ADVANCES IN Electrocardiography

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—ADVANCES IN—
Electrocardiography

Edited by

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Preface

For the past quarter century it has been our custom at New York University to teach electrocardiography in the most quantitative manner that the sum total of knowledge permitted at the particular time. An empirical approach has been avoided and the vicissitudes and pitfalls of electric anatomic correlations have been repeatedly stressed. In 1935, when the editor first had the privilege of working as a Voluntary Assistant in the Heart Station at Ann Arbor, the fundamental bases of electrocardiography had already begun to unfold from the remarkable mind of Frank N. Wilson and his loyal associates. A field of endeavor which seemed to have come to a permanently sterile end when Lewis left it in the 1920's had a vigorous renaissance and a surge of growth which continues to the present day.

Immediately after World War II, with young physicians returning to civilian life avid for knowledge, it was our task to present in 1946 and again in 1947 in the new Post Graduate Division of New York University College of Medicine a course which was titled "Advanced Electrocardiography" and advertised as being concerned with the fundamentals of electrocardiographic theory. Despite its emphasis on basic data and its content of analytical formulations, it was well attended and well received.

With the separation of the Post Graduate Division from the undergraduate school, the former becoming the New York University Post Graduate Medical School in December 1948, no further opportunity was presented to repeat the course, although others were and continue to be offered. In November 1955 the course was given by the editor alone in modified form under the auspices of the University of Miami and the Mt. Sinai Hospital of Greater Miami.

Late in 1955 a request was received from The American College of Physicians to prepare a course in electrocardiography for graduate physicians to be given at the New York University Bellevue Medical Center. It was agreed to do this provided that a completely fundamental rather than clinical or empirical approach would be acceptable.

This qualification was inserted in the agreement for several reasons. The most important of these was the obvious need for narrowing the considerable gap which had developed in the previous decade between the clinician on the one hand and the biophysicist, the physiologic engineer, the cellular physiologist, the clinical investigator and the instrumentologist on the other. In the period 1946–1956 advances in all fields of science were so rapid and at times so complex that even the physician with an intense interest in electrocardiography had difficulty keeping abreast of and comprehending the advances pertinent to the method. The purpose of the course was to present, interpret and integrate, so far as possible, these advances.

PART IV RHYTHMS

PART V

PART I SOURCE OF POTENTIAL, BIOELECTRICS OF THE MYOCARDIAL CELL

1 The Transmembrane Potential

CHARLES E KOSSMANN MD

When interpreting an electrocardiogram there are four parameters to be considered (fig 1) which determine the ultimate form of the record obtained These are (1) the source of potential (the heart), (2) the conductivity of the external medium (the body) (3) the size and shape of the boundaries of this medium (the surface of the body) and (4) the conductivity of the internal medium (the heart s blood)

The site of development of potential differences is the myocardial syncytial or cellular membrane The source of potential is the dissipation or restitution of a gradient of ions during myocardial activity which normally exists across the resting membranous barrier (Chapter 2)

A record of the gradient of potential across the resting cell wall cannot be made by an external lead because there is no flow of current in the surrounding medium due to the high impedance of the membrane As a consequence there is no electric field and the potential, V of any point in the medium is zero On the other hand if a discontinuity of the potential function can be achieved by passing an electrode into the myocardial fiber[1] it will assume the potential of the interior This can be demonstrated to be $-4\pi\phi$ where ϕ is the electrical moment of a unit area of the membrane In practice the membrane resting potential (MRP) as it is called can be measured either by inserting an exploring microelectrode into the cell with an indifferent electrode in the surrounding conducting medium or less precisely by injuring one end of the cell and pairing the indifferent electrode on that end with an exploring electrode on an uninjured portion (fig 2) The former method yields an intracellular potential whereas the latter yields an injury or demarcation potential To be noted in figure 2 is that similar polarity of the electrograms is obtained by opposite connections through the galvanometer in the two methods This arises from the circumstance that the first method yields the negative side of the resting membrane potential and the second in effect the positive side

With either method of recording a reduction in the impedance of the membrane caused by activity of the cell results in a loss of the ionic gradient and of the initial polarity of the membrane (depolarization activation

To be certain that prospective students understood what to expect, the following statement appeared in the announcement brochure

> The objective of the course will be to familiarize the student with the most recent advances in electrocardiography considered to be of the greatest immediate or future significance Since most of these advances have been of a fundamental nature the course itself must of *necessity be on a relatively fundamental* level Although the clinical implications of the newer electrocardiographic knowledge will be discussed exercises in clinical interpretation of records will not be included in the course

Under the circumstances it was expected that few physicians would apply Therefore it was somewhat of a surprise when the course was oversubscribed within a few days of its initial announcement in the Spring of 1956 This was interpreted to mean that the average internist's desire for recently acquired fundamental knowledge at least in electrocardiography, had been seriously underestimated Further this knowledge was not easy to come by in any single publication For these principal reasons a decision was reached to make the lectures with certain additions and deletions, available in this monograph

The editor acknowledges his gratitude to the faculty of the course and co-authors of the monograph for their expert and indispensable help and to Dr J Scott Butterworth who, during the course, presented his visual demonstration of the relationships between the origin of the cardiac potential and the potential of surface points We were fortunate in having Dr George Seiden then at the University of Pennsylvania, as one of the students He graciously presented a brief and lucid description of the cancellation technique for determining the electric heart center a technique which he had used extensively (Chapter 6) Dr Bertha Rader presented summary lectures on the Electrocardiogram and Serum Electrolytes and Electrocardiograms in Children but these have been omitted from the present monograph because of their availability in detailed form elsewhere

Some of the original investigations reported were made possible by the generous and greatly appreciated support of the Electrocardiographic Laboratory at New York University College of Medicine at various times by the Knapp Foundation of New York the New York Heart Association the Western New York State Heart Association the American Heart Association and the National Heart Institute of the U S P H S

Mr Nathan Marchand kindly reviewed and corrected the mathematical and analytical portions of the manuscript William Pisnosky made many of the line drawings and diagrams Drs Berger and Brumlik undertook the tasks of correcting proofs and making the index The Misses Muriel Luken and Sally Anna Evans capably *handled typing of the manuscript* The publishers were most generous in their help with the myriad of details concerned with publication

CHARLES E KOSSMANN, M D

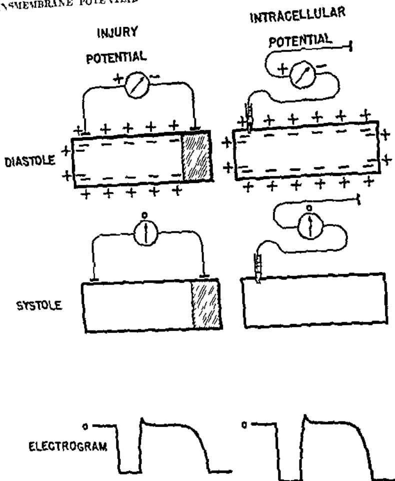


FIG 2 Diagram to illustrate the similarity of electrograms obtained by recording the injury potential (shaded area of cell is injured e g depolarized) and the intracellular potential The second electrode when recording the latter is assumed to be in a surrounding conducting medium distant from the cell The smaller magnitude of the injury electrogram is the result of loss of potential by short circuit through the surrounding medium

A typical ventricular transmembrane potential of the frog ventricle (Rana pipiens) recorded simultaneously with a bipolar lead from the forelegs is shown in figure 3 The monophasic action potential with a *total duration* inversely proportional to heart rate[3] may be subdivided into periods of depolarization (1-2 msec) *reversal* spike (6-15 msec) plateau and repolarization (fig 4) A short final phase of hyperpolarization (positive after potential) or *hypopolarization* (negative after potential) can probably exist at least pathologically (Chapter 16)

invasion, accession) The resting potential disappears (fig 3) A gradual restitution of the polarized state (repolarization, recovery, retreat, regression) restores the resting potential The form of the record, obtained by either method, during this series of events is essentially monophasic in nature When obtained with the microelectrode, it is called the monophasic action potential, the membrane action potential (MAP), or the transmembrane action potential

In passing, it should be noted that the earlier method of leading which *utilized an injured end of the cell as an "indifferent" electrode could easily* have been interpreted as yielding a record of "negativity" of the exploring electrode when, in truth, it represented a decreased positivity of that electrode This misinterpretation was probably the basis of the discredited "negativity hypothesis"

Resting potentials of cardiac membranes vary in magnitude from 40 to 110 mv, while the action potentials are some 20 to 50 mv larger The membrane action potential varies somewhat in form and duration depending upon the species studied,[4] the size of the orifice of the microelectrode[5] and the specific tissue studied (ventricular, atrial, or pacemaker tissue)

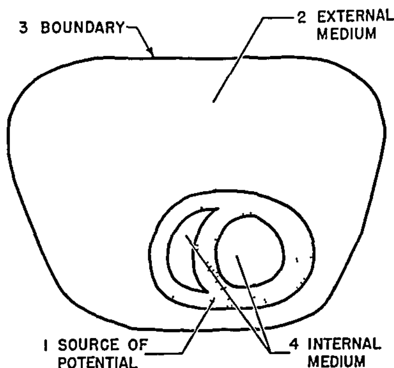


Fig 1 Diagrammatic cross section of the human thorax at the level of the heart summarizing the four principal parameters which determine the form of the electrocardiogram The internal medium 4 is the heart's blood and the external medium 2 the body tissues

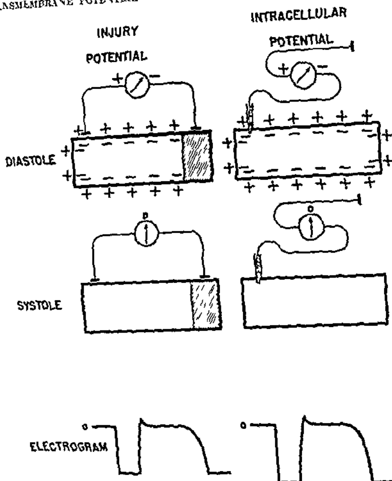


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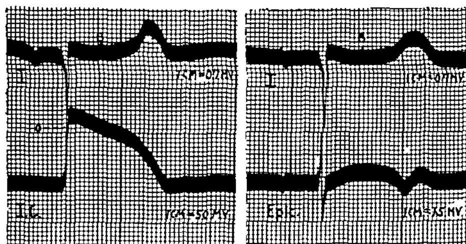


FIG 3 Ventricular intracellular potential (I C) and epicardial lead (Epic) from the same area as the microneedle was withdrawn recorded simultaneously with a bipolar lead from the forelegs (I) of Rana pipiens at 22 C To be noted are (1) the magnitude of the action potential (80 mv) as compared to the epicardial potential (RS deflection = 3 0 mv) (2) the three slopes of recovery of the action potential (3) the chance form of lead I simulating a first derivative (axial current) and of the epicardial lead a second derivative (membrane current) of the action potential with the S T segment of the latter elevated probably due to injury caused by the microelectrode The epicardial lead is distorted by AC pickup B is the deflection caused by excitation of the bulbus cordis Calibrations when recording are indicated on each record The zero level (0) of the MAP is measured from the upper border of the trace

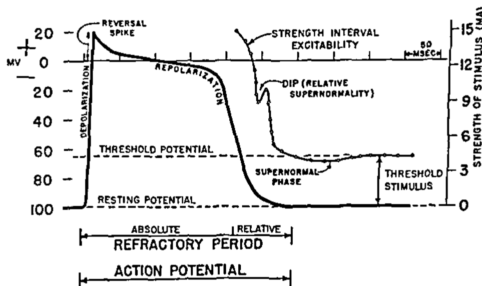


FIG 4 Diagram of an intracellular myocardial potential and the strength interval excitability curve of the same tissue (Chapter 15) The diagram is to serve as a concise glossary of terms rather than as an accurate representation of the transmembrane potential of any specific tissue or species (Modified from Brooks et al [4])

The recovery phase regarded as beginning at the peak of the reversal spike and ending with the return to the resting potential is incompletely understood from the viewpoint of what is happening in the membrane at the time (Chapter 2) Nevertheless, three different slopes of recovery can usually be recognized [5] These phases of recovery are of different rapidity the middle phase (plateau) being the slowest The first is the most sensitive to abnormal environments the last the least sensitive The different rates of recovery indicate different energy requirements for each of the phases

Simultaneous intracellular potentials from the atrium and the ventricle of a frog (fig 5) illustrate the shorter duration and steeper slope of repolarization in the former In pacemaker tissue the best studied being the Purkinje fiber of the dog depolarization is very rapid the reversal

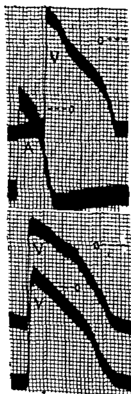


FIG 5 Simultaneous intracellular records of a frog heart made with two micro needles In the upper record one needle was in ventricular tissue (V) and the other in atrial tissue (A) in the lower record both needles were in ventricular tissue (V) Some artifacts are present but the figure does illustrate the different form of the MAP in atrial as compared to ventricular muscle Calibration 1 cm = 60 mv Time lines 0 04 sec

spike is higher and shorter, and the plateau is considerably longer at equivalent heart rates compared to myocardium Most characteristic, however, is the occurrence in diastole of a gradual loss of the resting potential ("prepotential") until the "threshold" level is reached, when rapid depolarization begins again (Chapter 11) This diastolic loss of potential accounts for the tissue's automaticity An example of the MAP of the sinoatrial node of the rabbit is shown in figure 6

Kleinfeld and Stein, working in this laboratory, have recently demonstrated that the duration of the action potential is shorter in the left atrium than in the right of the guinea pig (fig 7) This difference, if present in the human heart, probably accounts in part for the different behavior of these chambers in various hemodynamic states

For purposes of future reference (Chapter 15) the absolute and relative refractory periods and the threshold potentials are shown diagrammatically

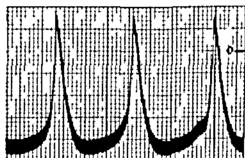


FIG 6 An intracellular potential made from the region of the sinoatrial node of the rabbit to illustrate what is believed to be a gradual diastolic loss of the resting potential (prepotential) There is some alternating current distortion of the record Calibration 1 cm = 25 mv Time lines 0 04 sec

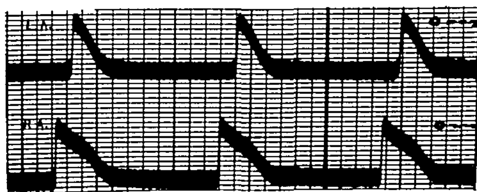


FIG 7 Simultaneous intracellular potentials from the left (L A) and right (R A) atria of the guinea pig illustrating the different forms obtained as a result principally of the shorter duration of the action potential in the left atrium Calibration 1 cm = 60 mv Time lines 0 04 sec

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4 Brooks C McC Hoffman B F Suckling E F and Orias O Excitability of the Heart New York Grune & Stratton 1955 Chap V
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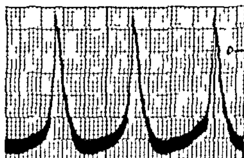


FIG. 6. An intracellular potential made from the region of the sinoatrial node of the rabbit to illustrate what is believed to be a gradual diastolic loss of the resting potential ("prepotential"). There is some alternating current distortion of the record. Calibration 1 cm = 25 mv. Time lines 0.04 sec.

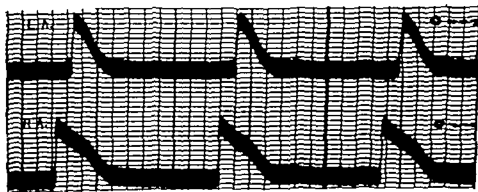


FIG. 7. Simultaneous intracellular potentials from the left (L A) and right (R A) atria of the guinea pig illustrating the different forms obtained as a result principally of the shorter duration of the action potential in the left atrium. Calibration 1 cm = 60 mv. Time lines 0.04 sec.

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2 Ionic Basis of the Transmembrane Potential

STANLEY A. BRILLER, M.D.

A CELL retains its uniqueness in large measure due to its membrane, which allows it to achieve a chemical composition differing from its environment. The relationship between the electric potential or voltage and the ionic milieu on the two sides of the membrane may be understood by examining the effects of connecting a battery to two plates which dip into two compartments of a container separated by an inert, semipermeable membrane (fig. 1). If the solution in the compartments on either side of the membrane contains equimolar concentrations of a salt such as KCl, it is apparent that the potassium cations will drift to the compartment containing the negative plate and the chloride anions to the positive plate. If we could arrange matters so that no chemical reactions would take place at either the anode or cathode it can be appreciated that after a given amount of time the concentration of potassium surrounding the cathode would be much greater than that about the anode (fig. 2). An opposite situation would apply to the distribution of the chloride ions. The point at which no further separation of ion species can be attained *is a function of the voltage applied. This relationship is expressed by the* Nernst equation

$$E = -\frac{RT}{ZF} \log_e \frac{Q_1}{Q_2} \qquad (1)$$

where E is the battery potential, R is the gas constant (1.987 calories per mole per degree), T is the absolute temperature, Z is the valency, F the Faraday (96,500 coulombs per equivalent), e is the natural logarithmic base, and Q_1 and Q_2 are the ionic concentrations in compartments 1 and 2 respectively.

This equation applies to anions as well as cations. As given, it will indicate the polarity in the Q_1 compartment due to the cationic disposition. The sign must be changed if predictions due to anionic displacement are *to be made or if cationic measurements are made in the Q_2 compartment.* Although the following statements apply with equal validity to both anions and cations, for simplicity only the potential measured in compartment Q_1 due to the cationic distribution (potassium ion) will be described. Movements and concentration of chloride are opposite but equal to potassium in this case.

In the example cited the equation applies only when a steady state of differential concentrations is attained. When the battery is first switched

on the concentrations of potassium within the compartments are equal and the calculated voltage (0) does not agree with that applied. Accordingly it is necessary to apply equation (1) only when equilibrium has been reached or else add expressions to indicate the effects of movement or flux of the ions across the membrane as follows

$$E = -\frac{RT}{ZF} \operatorname{Log} \frac{Q_1 F_1}{Q_2 F_2} \tag{2}$$

The symbolization in equation (2) is similar to that in equation (1). F_1 represents the flow of any one ion toward Q_1. F_2 flow in the opposite direction (fig. 3). When the battery in figure 1 is switched on F_1 for potassium greatly exceeds F and the equation will predict the voltage of the battery although the concentrations of ions have not had time to change appreciably.

In the example cited energy from the battery was supplied to the model and it should be noted that one of three possible situations may be detected: (1) $Q_1 = Q_2$ but F_1 is greater than F_2; (2) Q_1 is greater than Q and F_1 is greater than F_2; (3) Q_1 is greater than Q_2 and $F_1 = F_2$. The each position of ionic concentration and flow are characteristic of systems which are receiving energy from an outside source such as a battery.

When the battery is disconnected from the system the ions tend to flow in such a direction that equal concentration of ions in both compartment ultimately will be obtained. Until the latter situation is attained the polarity of the system remains unchanged. In the case of the potassium ion in the model system the flux ratio is reversed and F_2 becomes greater than F_1. Since the flux ratio is disposed oppositely to the concentration ratio the potential will be somewhat less than when F_1 was equal to F_2 in the equilibrium state. It is conceivable that if a battery were connected to this system in such a manner that the negative pole is attached to the Q compartment the potassium ions would be driven out of the Q_1 compartment at a greater rate than they tend to flow naturally. Under these circumstances the flux ratio will exceed the inverted concentration ratio and the polarity of the system will be reversed.

The discussion thus far indicates: (1) in general the polarity of an ionic system will be the opposite of the most highly concentrated ion contained in the compartment where the measurement is made; (2) if energy is delivered to such a system the net flow will be toward the greatest or potentially greatest concentration of ion species until equilibrium is reached; (3) if the system is delivering energy the net ionic flow will be away from the most concentrated ionic milieu. The potential will be lower in this case than in the equilibrium state; (4) if energy is supplied to a system in such a way that the flow away from the more concentrated environment is hastened the polarity may be reversed.

It has been assumed that there is a known and fixed value for the permeability of the membrane for the potassium ion However, it must be appreciated that another *species of ions might have more or less difficulty* in penetrating such a membrane by virtue of a difference in size as compared to potassium Moreover, as will be seen, a membrane may at times vary in its physical ability to restrain specific ionic movement In general, if several ionic systems are compared, that in which the permeabilities are greatest can supply the greatest ionic current or flux The freely moving ion in a complex system may thus swamp the effects due to the more sluggish members of the population

The Resting Biological System

The major charged constituents of cells are arranged as indicated in figure 4 It might be supposed that the cell membrane is completely impermeable to protein and sodium, at least in the resting state, and that

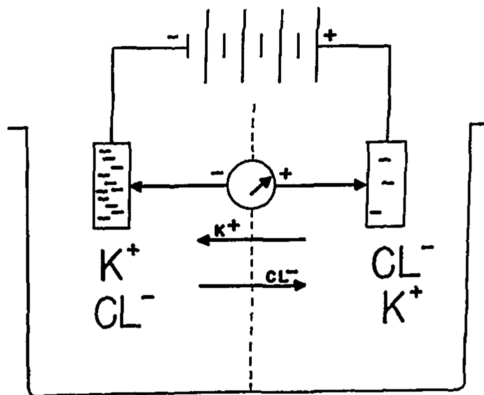


FIG 1 Disposition of ions at the instant of application of potential across a semipermeable membrane (dashed vertical line) separating equimolar concentrations of potassium chloride Compartment *Q* (see text) is to the left Dashes within electrodes *indicate relative* electron concentrations Circle containing arrow represents a polarity indicating galvanometer Horizontal arrows indicate *net* flow

FIG 2 Same as fig 1 *after equilibrium* between applied potential and ionic concentrations has been reached

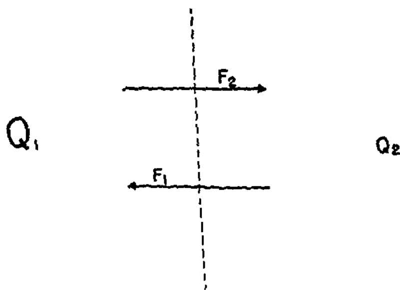


Fig 3 Schematic representation of equation (2) at equilibrium

since the resting cell interior is some 100 millivolts negative to the outside, the concentration ratios of potassium ion (and chloride ion) adequately *account for the magnitude and polarity of the observed potential* Such a premise might be strengthened by a number of observations (1) If the external concentration of potassium is changed, the observed potential agrees almost exactly with the potential calculated by equation (1) in which the internal concentration of potassium is unchanged but in which the experimental values of the altered external concentration are inserted [1] In such experiments sufficient time must be allowed for a new flux equilibrium to be achieved after the extracellular potassium concentration is altered [2] It is assumed that any net gain or loss of intracellular potassium is accompanied by similarly directed water movement permitting the *concentration* of intracellular potassium to remain unaltered (2) The presumption of flux equilibrium for potassium has been confirmed by the use of radioactive tracer studies [3] Although these experiments were performed on isolated tissue in which there is an apparently unavoidable loss of potassium, the calculated potential agrees with the measured when

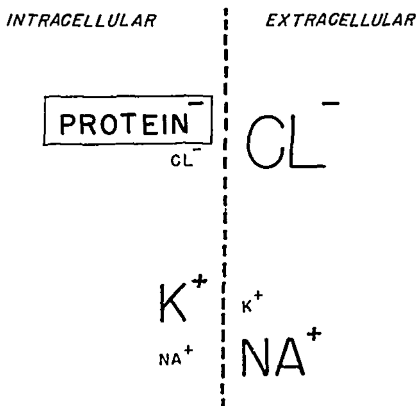


Fig 4 Relative concentrations of certain constituents of the intra and extra cellular spaces indicated by the size of the symbols

the flux inequality is introduced into equation (2) (3) The foregoing experiments indicate that potassium penetrates the cellular membrane freely (4) Chloride ion acts in a manner entirely comparable to potassium [4]

It can be seen that far from generating a potential across the cell membrane these ions act as though a battery which supplied the energy for keeping them in place were connected across the membrane Most present day electrophysiologists believe that energy for this purpose is delivered to the cell through the agency of the sodium ion Such evidence is deducible from tracer experiment with radioactive sodium It was found that although the cell membrane is some 30 times less permeable to sodium than to potassium ion the former passes across the membrane in considerable number [4] Hence the resting cell membrane cannot be thought to be impermeable to sodium

Reference to equation (2) reveals that by its concentration ratio alone, the low intracellular and high extracellular concentrations of sodium might be thought to produce a potential whose polarity is the opposite of that observed There is only one way to reconcile this paradox in view of the appreciable permeability of the membrane to sodium the inward flux (F_1) of sodium ion must be 50 to 100 times that of the outward flux (F_2) Radioactive tracer studies however have revealed a ratio many times smaller [4] Indeed these studies confirm the fact that the intact resting cell must be in sodium balance If it is presumed that the inward flux of sodium is in ionic one but that an equivalent amount of sodium is [illegible] across the membrane in non ionic form the *ionic* flux ratio would agree with the predicted ratio The exact manner in which sodium might be expelled from a cell is not known Terms such as active transport and sodium pump have been used to describe the process A theoretical scheme outlined by one group of investigators[4] is presented in figure 5 Here an intracellular substance (P) combines with intracellular sodium ion and the combination passes across the membrane in un ionized form In the extracellular compartment dissociation of the PNa combination is much favored because of the great affinity of ground substance (GS) for P Sodium ion is thereby free to rediffuse into the cell The other constituents of the extra and intracellular compartments are distributed in accord with the potential developed by the active transport or pumping of sodium

On the basis of its physical and chemical properties and its distribution in tissue histamine has been proposed as being a likely pump substance [7] It might be added that 5 hydroxytryptamine (serotonin) is at least as likely a candidate Whatever the mechanism responsible for the extrusion of intracellular sodium it appears that metabolic energy is introduced at

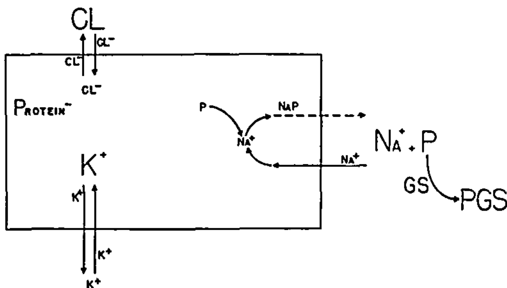


Fig 5 Equilibria across the resting cell membrane The dashed arrow indicate non ionic flux P is pump substance GS is ground substance

this point Whether it is expended by the ATP induced synthesis of a pump substance or some other modality is a matter of much speculation

The Active Biological State

Maintenance of the resting potential of a cell has been shown to represent a manifestation of the expenditure of metabolic energy in bringing about a unique separation of the monovalent ionic constituents of the cell The active state will be seen to demonstrate the results of allowing this separation to lapse in a carefully integrated manner

Hodgkin, Huxley and Katz[5] demonstrated that the greater impermeability of the resting membrane to sodium can be abruptly abolished by reducing the resting potential electrically Such a reduction in potential may be brought about by a natural or artificial pacemaker or by currents from an adjacent active cell The effect of allowing freer flux of sodium ion across the cell membrane (which maintains its resting semipermeability to potassium) is that the sodium pump mechanism becomes overwhelmed Consequently, there is relatively free movement of sodium ions in both directions across the membrane although inward movement of this ion predominates[3] Unrestrained sodium movement impelled by its concentration gradient is therefore able to deliver free energy to the cell in the form of electrical potential which tends to make the inside of the cell less negative Such a change in potential in turn makes the membrane more permeable to sodium and, coupled with the presumed inactivation of the sodium pump mechanism, the intracellular potential rises past zero toward

the level predicted by equation (1) for sodium ion.[8] It should be noted that during this process the cell gains a number of sodium ions. However the net gain is an infinitely small proportion of the sodium already there.[9]

As the movements of sodium ions across the membrane reach a peak (at which time the intracellular potential is positive in polarity) the membrane gradually begins to increase in permeability to potassium. These latter ions, impelled by the hostile positively charged intracellular environment, leave the cell in greater numbers than they enter. These free movements of potassium (coupled with the now decreasing permeability of the membrane to sodium) reduce the positive potential within the cell.

Finally, as the relative impermeability of the membrane to sodium is completely re-established, potassium flux dominates once again and the intracellular potential resumes its negative polarity. During the later phases of the "active state," the potassium permeability gradually declines to its previous level. Such changes in sodium and potassium permeability and intracellular potential for a nerve cell[10] are shown in figure 6.

It will be recalled that the cell has gained sodium and lost an equivalent amount of potassium in passing through the active state. Reactivation of the sodium pump, with subsequent extrusion of sodium and re-entry of potassium, occurs promptly and is synchronous with varying degrees of nonresponsiveness of the cellular mechanism known as the absolute and relative refractory period (Chapter 1). It will also be appreciated that as applied to electrocardiography hyperpermeability to sodium dominates

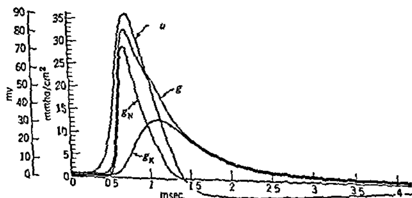


FIG. 6. Calculated action potential (v) and ionic conductances (g_K potassium, g_N sodium, g total conductance) of a propagated nerve impulse. The specific conductances above may be regarded as synonymous with the specific permeabilities discussed in the text. That portion of the voltage rise occuring before ion conductances have changed is contributed by an external pacemaker and by charge stored in the membrane capacity. Note that the voltage ordinate is scaled with the resting potential regarded as zero. (From Hodgkin and Huxley, J. Physiol.[10])

during QRS, whereas the T wave is probably ascribable to the movements of potassium across the cellular membranes

Although the fluxes of sodium and potassium have been well documented in a series of elegant experiments by Keynes, Lewis, Hodgkin and others,[3, 5, 8, 9, 10] the nature of serial changes in membrane permeability which regulate the fluxes of these two ion species is unknown. Wilson and Nachmansohn[11] believe that acetylcholine is implicated in causing alterations in the molecular structure of the membrane during activity. Others[5] indicate that the amount of heat generated during activity is too small to suggest an origin other than that due to movement of ions through the membrane. Although calcium ion, a most necessary ingredient for nerve and muscle function, apparently plays no direct role in generating the transmembrane potential, *it is believed to be active in regulating membrane permeability*.[6] *Despite numerous theoretical studies*[1] *in which charged* and uncharged pores within the membrane have been considered, no artificial membrane has yet been devised which can duplicate the delicate and selective control exhibited by the nerve membrane of the lowly squid.

No attempt has been made in the foregoing to compare ionic mechanisms in muscle and nerve. Because of its size and accessibility, the giant axon of the squid can be studied intimately and has provided the least controversial data. Not all squid axon studies may be repeated with muscle and other tissues without generous assumptions. A complete comparative discussion of the behavior of these various tissues may be obtained in a recent monograph by Harris.[13]

The mechanisms given for the ionic origin of the transmembrane potential apply to a great, although variable, degree to all tissue. A given experiment showing anomalous behavior requires considerable modification of this simple theory and often requires complex mathematical interpretation. The suggestion[14] that sodium ion (and possibly potassium ion) may be partly bound to the membrane surfaces constitutes an example of such a situation.

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3 Experimental Modification of the Transmembrane Potential, Relation to Myocardial Mechanics, Alternation of the Action Potential

MORRIS KLEINFELD, M D

Value of Studying Direct Transmembrane Potentials

THE APPLICATION of the intracellular capillary electrode to single myocardial fibers has provided a new tool for studying the effects of temperature, tension, ionic concentrations, drugs and induced arrhythmias on the transmembrane potential of cells The observed alterations have provided a better understanding of (1) the nature properties, and fundamental importance of the myocardial membrane to electrical and mechanical activity, (2) the basic mechanisms underlying the action of drugs and arrhythmias, (3) the loci of action of some of these drugs (4) the relationship between electrical and mechanical events with the membrane in different environments, (5) the relationship between derangements of cellular metabolism and function, (6) the role of neuroeffectors in the mediation of chemical effects and (7) the nature of cardiac excitability myocardial failure, cellular block and such phenomena as electrical alternans and spontaneous rhythmicity in pacemaker tissue

Factors Which Modify the Transmembrane Potential

Temperature

Quantitative measurements of the effects of temperature on individual fibers of the hearts of various species have been made by a number of workers[1,2] The temperatures to which mammalian tissues have been exposed range from 4°C to 50°C in cold blooded animals the usual range has been from 2°C to 30°C

When electrodes were placed in pacemaker tissue (fig 6 in Chapter 1) to record the typical prepotential (the upward movement of the voltage time curve starting some 50 to 100 msec before the upstroke of the propagated action potential), it was observed that a fall in temperature slows the potential time course in all its phases but does not have any appreciable effect on the threshold potential for spontaneous firing nor on the shape of the action potential until the greatest extremes of temperature are reached[2]

The magnitude of the resting transmembrane potential and of the reversal potential or 'overshoot' are not changed appreciably at temperatures within the range of 25° to 40°C Beyond these limits, both the rest

ing potential and the overshoot decrease[2] A lowering of the temperature from 25° to 16°C produces a much greater change the amplitude of the action potential falls from 120 mv to 40 mv and the membrane potential fall from 90 mv to 55 mv[3] Heating accelerates and cold retards spontaneous depolarization in pacemaker tissue

In the frog ventricle, over a range of 2 C to 30 C no effect on resting potential could be observed[1] With decreasing temperature there is an increase in depolarization time a prolongation of the duration of the action potential with merging of the first and second recovery phase Trautwein[3] showed that even when the heart is driven at a constant rate (55 beats/min) similar degrees of cooling (40 to 25°C) prolong the duration of the action potential (APd) to 950 msec

Heart Rate

In experiments on the dog s ventricle at rates from 60 to 250 beats per minute the relationship between electrical activity and frequency of contraction is linear[4] A similar relationship has been observed between the duration of the transmembrane action potential of a single ventricular fiber and the frequency of contraction Woodbury s and our own studies demonstrate a similar linear relationship in the frog heart (fig 1)

There is a predictable maximum limit to the linear relationship between heart rate APd and the Q T interval of a surface electrocardiogram In the dog for example this linear relationship is lost at a frequency somewhere between 250 and 300 beats per minute at these rates shortening of the action potential approaches a limit Linearity also ceases to exist at excessively low rates

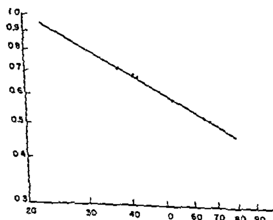


Fig 1 Duration of action potential (frog ventricle) in seconds (ordinate) as a function of heart rate per minute (abscissa) (From Kleinfeld Stein and Meyers Circulation Res[1])

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Inorganic Ions

Potassium The effect of an alteration in the concentration of extracellular potassium on the action potentials of single fibers of papillary muscle Purkinje tissue and atrium are similar Increased K causes a slowing of the rise a decrease or complete loss of the reversal of polarity and a shortening in the duration of the action potential In the frog ventricle, an increased concentration of KCl was shown by Woodbury and Hecht[11] to cause a decrease in the membrane resting potential also A lowering of the potassium concentration resulted in a similar minor change in the action potential It has been suggested that the mechanism by which these effects are produced seems to be related to the change in resting potential and is not a direct action of the ion on the excitatory process [5] It is noteworthy that injections of small quantities of KCl into the squid giant axon by microinjection showed a minimal effect on the membrane potential [12]

Calcium The action potential has shown great differences in sensitivity of the various tissues studied When the extracellular Ca is increased to four times normal the form of the action potential of the Purkinje fiber shows no change in the slope of the prepotential but the MRP is decreased On the other hand at a similar level of Ca the action potential of atrial and papillary muscle are drastically altered In the case of the atrium, a change in configuration similar to that produced by acetylcholine occurs The initial stages of repolarization are greatly accelerated, on the other hand the action potential terminates in a prolonged positive after potential similar in shape to that normally recorded from skeletal muscle [5] The change in the action potential of the ventricle is of a similar nature The plateau characteristic of this tissue is lost and repolarization proceed with a time course similar to that found in normal atrium

Low calcium has quite the opposite effect The atrial action potential is prolonged and a plateau often appears between the initial reversal and the phase of repolarization In the ventricular muscle the duration of the plateau is considerably increased the rate of repolarization however is relatively unchanged (fig 2) In the presence of low calcium the atrial action potential is indistinguishable from that of a normal ventricular fiber High Ca on the other hand converts the ventricular action potential to a shape resembling that of a normal atrial fiber These findings suggest that the differences in form of the MAP normally displayed by these two tissues of the heart may include a difference in sensitivity to Ca of the respective fiber membranes [5]

Magnesium Strontium and Barium Magnesium has little effect on the transmembrane potential in the presence of normal amounts of Ca When the latter ion is decreased a considerable shortening of the APd is observed, similar to that resulting from an excess of Ca [5] Strontium acts in the same

The transmembrane potential recorded from a single fiber of the isolated papillary muscle behaves like the intact heart However, at excessively rapid rates a new change, incomplete repolarization, supervenes The excessive rate prevents complete recovery and the resting and action potentials decrease in magnitude [5]

Initial Tension

The effect of initial tension on the response of the atria of rats was investigated by Hollander and Webb [6] The initial, or resting tension on the atria was changed in steps from 250 mg to 1250 mg and the membrane and contractile characteristics at each tension were studied The developed tension increased with the initial tension, but this was not accompanied by *any detectable change in the membrane potential* The authors suggested that the effect of altering initial tension on the contractile process was directly upon the contractile elements and was not mediated through changes in the electrical behavior of the cardiac cells They stated that the coupling between excitation and contraction is probably exerted in one direction only, contractile processes may vary independent of membranous processes A change in the isometric tensions recorded from the papillary muscle of the dog similarly did not alter the magnitude of the membrane resting potential

Autonomic Nerves and Chemical Mediators

Vagal Stimulation and Acetylcholine Repolarization of the dog's atrium is greatly accelerated by stimulation of the peripheral end of the vagus and by acetylcholine This acceleration results at times in completion of recovery within 10 msec The resting and action potentials are unaffected The transmembrane potential of the dog ventricle is not affected as long as the heart is driven at a constant rate [7] Studies on the embryonic chick heart however, have shown a decrease in both the resting and action potential following the administration of acetylcholine [8] The difference in results may represent a species difference

Vagal stimulation causes a decrease in the slope of the slow depolarization which occurs preliminary to a propagated action in pacemaker fibers [9] Stoppage or slowing of the heart by means of vagus nerve stimulation can be explained on this basis

L Epinephrine L Epinephrine increases the rate of repolarization and shortens the APd of isolated papillary and atrial muscle of the dog No significant change in resting potentials occurs [5] These results are in general agreement with those Fingl et al [8] obtained using the chick embryo and frog heart In isolated rat atria Webb and Hollander [10] however, observed a slowing rather than an increase in the rate of repolarization

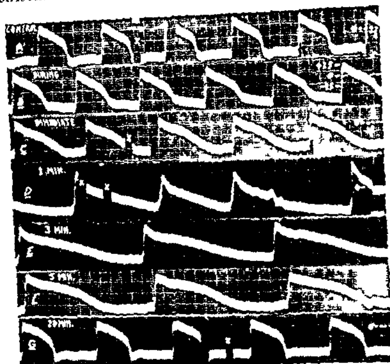


FIG 3 Effect of barium chloride (5 mg/kg) injected into the aorta on the membrane action potential of ventricular fibers of the frog heart Ordinates millivolt abscissae time Time line 0 04 second All measurements made from top of string shadow X indicates mark where standardization voltage was introduced See text for discussion (From Kleinfeld Stein and Meyers Circulation Res)

manner as calcium[14] Barium conspicuously increases the duration of the ventricular action potential of the frog heart even at normal Ca level [14] This can be seen in figure 3

Sodium and Lithium A decrease in extracellular Na concentration produces a decrease both in the rate of rise and in the magnitude of the transmembrane action potential with loss of overshoot In addition in pacemaker fibers the rate of impulse formation is slowed as a result of a slowed rate of diastolic depolarization[15] In a concentration 10 per cent to 20 per cent below normal spontaneous activity in such tissue ceases and propagation of the action potential fails The changes are all promptly reversed when the sodium concentration is increased to normal levels Although the changes produced in the action potential are profound, alteration of the extracellular Na concentration has little effect on the magnitude of the resting transmembrane potential Cranefield et al[16]

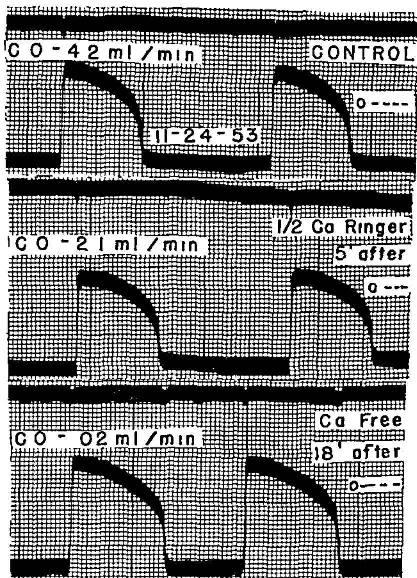


FIG 2 The effect of decreasing extracellular calcium on the electrical and mechanical activities of the isolated perfused frog ventricle Simultaneous records are of the indirect bipolar electrogram (above) and the single fiber membrane action potential (below) Cardiac output (C O) was taken just prior to recording of the electrical potentials Ordinates millivolts abscissae time Time lines 0 04 sec Gain 0 9 cm = 50 mv for intracellular potential for indirect electrocardiogram 1 0 cm = 1 mv

All measurements were made from the top of the action potential trace Dotted lines indicate zero level of potential (0) for the membrane

were required to produce electrical effects The most consistent change was a shortened APd and decreased voltage The results were more marked in the presence of low Na Lithium did not modify the effect produced by low or high concentration of Na (fig 4)

Drugs

Cardiac Glycosides The effects of a number of cardiac glycosides (digitoxin ouabain lanatoside C etc) on the transmembrane potential of the normal frog heart in situ are essentially similar The major effects as noted by Woodbury and Hecht are (1) repolarization is profoundly altered the duration of the membrane action potential being greatly shortened but the duration of depolarization not affected (2) after toxic doses of digitoxin (1–2 mg/kg) the record assumes a spike like appearance (3) recovery in some instances commences before depolarization has been completed and the depolarization deflection appears prematurely arrested (undershoot) These changes were independent of mechanical events Physical movements recorded simultaneously with the membrane action potential remained relatively unchanged in the face of pronounced alterations in the latter

The steepening of the first phase of repolarization of the membrane action potential showed a high correlation with the magnitude of the S T segment depression in the simultaneously recorded surface electrogram [11] Our studies have yielded results similar to those observed by Woodbury and Hecht (fig 5)

The similarity in effect of decreased extracellular Na and of digitalis has been observed by Draper and Weidmann[13] on isolated Purkinje tissue No consistent change in the resting potential was noted however

Antimetabolites A number of enzyme inhibitors such as cyanide dinitrophenol fluoroacetate and iodoacetate have been extensively studied by others [18, 19] Our investigations extended these studies to single ventricular fibers of the frog s heart the most detailed being carried out with iodoacetate [20] The following is a summary of our findings and conclusions

Prominent changes in both the electrical and mechanical properties were observed The most consistent and earliest of these was a shortening of the duration of the action potential (APd) this was progressive Coincidentally a shortened S T interval and abnormal T wave were observed in the indirect electrocardiogram Of lesser frequency and occurring late was a prolongation of the P R interval The height of the MAI slowly decreased with impaired depolarization occurring as a relatively late phenomenon (fig 6) The changes in mechanical activity were represented by a progressive decrease in cardiac output and stroke volume Atrial activity persisted for 10 to 20 minutes after ventricular arrest The early

observed similar changes in the turtle ventricle when the extracellular sodium concentration was lowered

Injection of small quantities of NaCl intracellularly by Hodgkin and Keynes[1] reduced the action potential of the squid axon

Lithium in proper concentrations was shown by Weidmann to be a substitute to some extent for Na In our studies on the isolated perfused frog heart,[17] relatively high concentrations of LiCl (67 mEq /L and above)

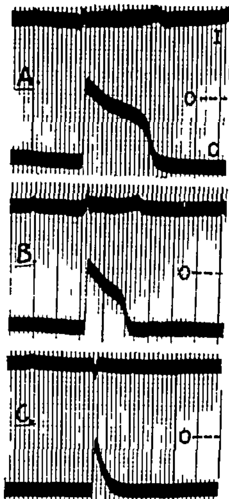


Fig 4 A Control record of the intracellular potential (c) taken simultaneously with the bipolar electrocardiogram (I) of the isolated frog heart perfused with Ringer's solution B 67 mEq /L lithium chloride added to Ringer's solution C 67 mEq /L lithium chloride replacing sodium chloride of Ringer's solution Discussion in text Ordinates millivolts abscissae time Time lines 0 04 sec Gain 0 9 cm = 50 mv for intracellular potential 1 0 cm = 1 mv for lead I All measurements made from top of string shadow Dotted lines indicate zero level of potential (From Stein Kleinfeld Greene and Myers Am J Physiol [17])

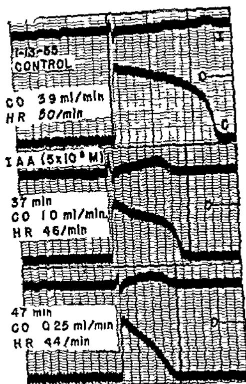


Fig 6 The effect of 5×10^{-4} M *Iodoacetate (IAA)* administered as a perfusion on the electrical and mechanical activities *of the* isolated frog heart Simultaneous records are of the indirect electrocardiogram *(I) and the* single fiber membrane action potential (C) Cardiac output (C O) and heart rate (H R) were taken just prior to recording of the electrical potentials Ordinates millivolts abscissae time Time line 0 04 sec Gain 0 9 cm = 50 mv *for* intracellular potential for indirect electrocardiogram (I) 1 0 cm = 1 mv

All measurements were made from the *top of* the action potential trace Dotted line indicates zero level of potential *(0) for* th membrane (From Kleinfeld Stein Magin and Ko mann J Clin Invest[26])

which has been shown by *Hodgkin* and *Keynes*[12] to block the efflux of 24Na introduced into the squid axon by microinjection

Local Anesthetics Local anesthetics are said to "stabilize" excitable membranes in view of the following (1) stronger currents are *needed* to stimulate the tissue *(2)* spontaneous rhythms are slowed or suppressed, (3) conducted impulses *may* be blocked but (4) the resting potential remains practically unchanged

As a basis of obtaining a better *understanding* of the mode of action of these stabilizing agents Weidmann[21] *studied* the effects of such substances as cocaine hydrochloride (16 mg /ml) procaine amide (50 *mg* /ml), quinidine

alterations in contractility of the ventricles were usually paralleled by changes in the repolarization phase of the action potential (shortened APd). The observation makes it difficult to ascribe quantitative differences in energy requirements to these two cardiac functions as has been postulated.[19]

The addition of substrates, pyruvate (0.0055M) and acetate (0.0055M), to the IAA perfused heart produced only a partial recovery and delay of ultimate deterioration of cardiac activity. A similar result was obtained when adenosine triphosphate (1.0×10^{-4} M) was added. Doubling the concentration of these substances did not significantly alter the results. The inability of these metabolic intermediates to restore cardiac activity suggests that IAA has actions other than specific inhibition of triosephosphate dehydrogenase.

It is postulated that the enhanced repolarization is associated with an increased migration of potassium out of the cell during its electrical activity.

The decrease in MAP with loss of overshoot observed is a late event may well be due to an inactivation of the sodium carrying mechanism (Chapter 2). In this manner, it may act similarly to dinitrophenol (DNP),

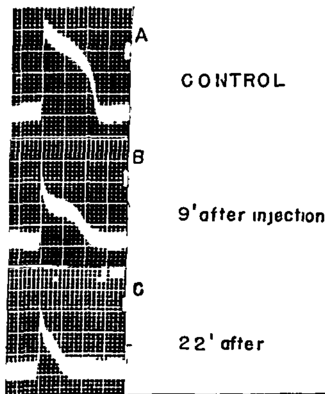


FIG 5 The effect of digitoxin administered as a perfusion (1.2 mg/kg) on the transmembrane potential of the frog ventricle. Gain 0.9 cm = 50 mv. Zero level at upper border of white bar at right of each trace.

In studies on isolated rat atria, Hollander and Webb[6] found no correlation between developed tension and the magnitude of resting or action potentials but did observe a correlation between the degree of contraction and time course of the action potential. The latter was expressed in terms of the duration and area of the action potential. Since the depolarization time remains fairly constant, these depend primarily on the rate of membrane repolarization. Such a correlation has been implied also in work on various cardiac preparations with regard to the action of the vagus or cholinergic esters and in our studies with antimetabolites.

In other studies undertaken in this laboratory an apparent dissociation between electrical and mechanical activity was noted. In experiments involving a progressive decrease of calcium in the perfusate a condition was observed where no cardiac output was obtained in the presence of a normal propagated action potential (fig. 2). The mechanism underlying this uncoupling of membrane phenomena from the usual contractile response has not been elucidated. The difficulty is due to the complexity of the coupling process and to the many factors which are known to influence the contractile proteins responsible for the development of tension.

From the studies of Sandow,[20] it is believed that in skeletal muscle, at least, the excitation contraction coupling does not depend on local ionic current or on sodium ions that have entered the cell during depolarization. Sandow states that the sudden depolarization of the membrane might serve as a trigger mechanism for initiating the contractile response. He also discussed the possibility that release of Ca from the depolarized membrane might be the coupling link and that these ions might diffuse inward to act on the contractile systems. This may very well explain the dissociation observed in the experiment involving low calcium: sufficient Ca is not available for the necessary coupling of the electrical and mechanical events. Whether Sandow's concept for skeletal muscle applies to cardiac muscle cannot at present be said. It does appear, however, as Hollander and Webb[6] have stated, that the concept needs some modification relative to heart muscle and further research along this line is essential.

ALTERNATION OF THE MEMBRANE ACTION POTENTIAL

The phenomenon of electrical alternans was first described in the experimental animal by Hering[3] in 1908. Lewis[4] in 1910 reported its occurrence in man during a bout of paroxysmal atrial tachycardia. A number of investigators have since produced this phenomenon experimentally and have explained its mechanism as well as its relationship to mechanical and pulsus alternans.[24,25] All types of electrical alternans have been reported involving variations in amplitude, direction or both of the deflections. Kisch[25] pointed out that electrical alternans may also involve

sulfate (10 mg/ml), and diphenyl hydramine hydrochloride (an antihistamine, 10 mg/ml) on the electrical potential of mammalian Purkinje fibers. All of these agents (1) stopped spontaneous activity within a few minutes, (2) blocked conduction after 1 to 2 hours, (3) lowered moderately the rate of rise and overshoot of the action potential, but (4) had little effect on the diastolic membrane potential. Normal values could be restored if the membrane potential was increased to about 120 mv previous to passage of an impulse. The author suggested that the lowered rate of rise and overshoot are associated with an inactivation of the sodium carrying system. To ascribe antifibrillatory action to them from their effect on relatively normal Purkinje fibers is, however, not warranted (Chapter 10).

Relation of the Transmembrane Potential to Myocardial Mechanics

The mechanical activity of cardiac tissues is evoked by the propagated action potential and occurs with a brief latency after depolarization of the membrane.

A relationship exists between depolarization and repolarization of the fiber membrane, on the one hand, and contraction and relaxation, on the other, as shown in figure 7. It can be seen that the peak tension is reached simultaneously with the end of the plateau of the transmembrane potential and repolarization precedes relaxation by only a short interval. This suggests that the two phenomena may be causally related. On the other hand, records obtained under such conditions as digitalis intoxication and following the administration of antimetabolites and acetylcholine show that repolarization is often completed long before the onset of mechanical relaxation. Thus, an immediate cause and effect relationship between the two phenomena is not invariably present.

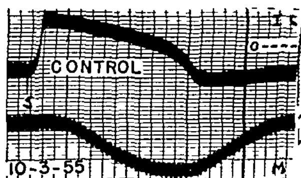


Fig. 7. Transmembrane action potential and myogram recorded from a ventricular strip of frog heart showing latency between depolarization and onset of contraction. S, stimulus; I.C., intracellular potential; M, myogram. Time lines 0.04 sec.

the intervals of the electrocardiogram There has been no reported incidence of electrical alternans simultaneously involving the atria and ventricles The most frequent form affects the ventricular complexes only alternation of the P wave is rare

Although Schutz[29] in 1936 produced alternation of the monophasic injury potential (demarcation potential) (see fig 2 in Chapter 1) the demonstration of alternation of the membrane action potential of ventricular fibers was recently reported from this laboratory for the first time[30] In intact frog hearts the agents used were injected into the aorta When isolated ventricular strips tied to a tension spring and immersed in oxygenated frog Ringer s solution were used, the agents were added to the bath

Electrical alternans was observed following the administration of varying concentrations of L-thyroxine or triiodothyronine (TIT) in 13 of 37 experiments It was observed in one instance after the induction of acute anoxia produced by cutting off the oxygen supply to the perfusate The most frequent association was with triiodothyronine (8 of 20 experiments)

In experiments on the intact heart this phenomenon occurred both with normal and slow rates It was also present with normal or depressed cardiac contractility but more frequently with the latter The alternans was of transient character and not infrequently followed a worsening of the electrical activity such as the development of varying degrees of A V block and bizarre ventricular complexes During these events the mechanical activity showed impairment of function terminating usually in asystole In approximately 30 per cent of the experiments there was a return to normal electrical and mechanical activity from 10 minutes to 90 minutes after onset

Although the electrical alternation usually involved more than one phase of the action potential four fairly distinct types were observed These were alternation in (1) the rate of depolarization (2) the rate of repolarization (3) the magnitude of the membrane action potential and (4) hyperpolarization In two experiments electrical alternation was observed in the indirect bipolar electrocardiogram without a similar occurrence in the single fiber studied simultaneously (fig 12)

The following is a summary of the changes observed

1 Alternation in rate of depolarization Figure 8B demonstrates the changes characteristic of this group The membrane action potential shows alternation in the rate of depolarization with the height of the membrane action potential essentially unchanged There is also a variation in the duration of the action potential The heart rate is moderately slowed as compared to the control (A of fig 8) The indirect bipolar electrocardiogram also shows electrical alternation The record taken 35 minutes after

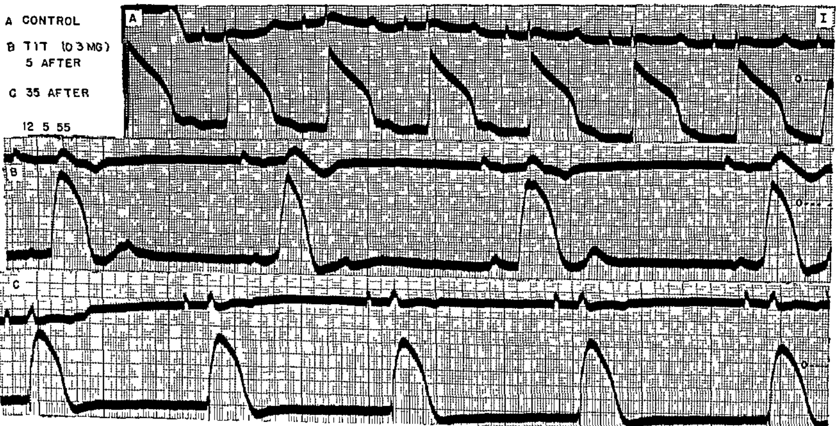


FIG 8 The effect on the action potential of the intact frog heart of 0 3 mg Triiodothyronine (TIT) injected directly into the right branch of the aorta Simultaneous records are of the indirect bipolar electrocardiogram (I) and the single fiber membrane action potential (Cp) Ordinates millivolts abscissae time Time lines 0 04 sec gain 1 4 cm = 50 mv for intracellular potential for indirect electrocardiogram (I) 1 0 cm = 1 mv All measurements were made from the top of the action potential trace Dotted line indicates zero level of potential (0) for the membrane (From Kleinfeld Stein and Magin Am J Physiol [9])



Fig 10 Alternation in magnitude of the action potential of the frog heart following administration of 0 4 mg L Thyroxine Bipolar electrocardiogram above membrane action potential below Time line and zero of potential as in figure 8 Cam 0 9 cm = 50 mv for the intracellular potential for indirect electrocardiogram 1 0 cm = 1 mv (Kleinfeld Stein and Magin [30])

alternate beat There is also alternation of the form of the T wave in the indirect bipolar electrocardiogram the notched T wave occurring simultaneously with the greater degree of hyperpolarization The configuration magnitude and duration of the other phases of the action potentials are essentially similar

Electrical alternans was first described in the frog by Mines [6] in 1912, and he suggested that the phenomenon was due to a lower excitability of a portion or segment of the heart muscle Brody and Rossman [7] suggested that it may be the result of two alternating foci of impulse initiation or of two alternating paths of conduction from one focus Katz [31] stated that the factor underlying all forms of cardiac alternation is a marked prolongation of the refractory phase of some part of the heart Following a normal activation a succeeding impulse finds some regions of the myocardium still refractory hence the response of every alternate beat will be electrically or mechanically abnormal

Considerable controversy exists concerning the occurrence of electrical alternation without mechanical alternation and vice versa It has been stated by a number of investigators [5, 26] that while portions of the heart muscle may be in a state of diminished excitability leading to alternation

TIT administration (C of fig 8) still shows abnormal complexes as compared to the control (A of fig 8) but no alternation

2 Alternation of repolarization Figure 9B best exemplifies this change Each alternate membrane action potential shows a repolarization phase somewhat different in form from the succeeding one The duration of the latter also vary The magnitude of the action potential does not alternate but is significantly decreased as compared to the control (A of fig 9) This record shows alternation also of the mechanical activity (B of fig 9)

3 Alternation in magnitude of the membrane action potential The most conspicuous finding is an alternation in the magnitude of the membrane action potential This is best illustrated in C of figure 10 Concomitant with this, there is alternation in the rates of depolarization and repolarization The action potentials of lesser height show an absence of overshoot The indirect bipolar electrocardiogram also demonstrates electrical alternation involving the QRS complexes and T waves The heart rate is essentially unchanged from the control record (A of fig 10) Ten minutes after injection of 0.4 mg l-thyroxine (D of fig 10) there is a marked slowing of the heart rate but no alternans

4 Alternation of hyperpolarization This phenomenon is illustrated in figure 11 which shows hyperpolarization of different degree with each

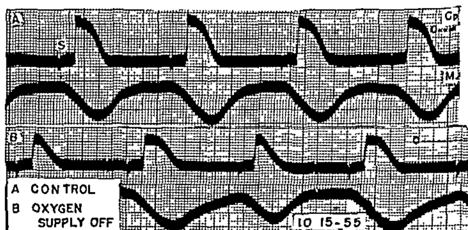


Fig 9 The effect of anoxia on the electrical and mechanical activity of the isolated ventricular strip A) Control record The heart muscle was driven by a Grass stimulator at a fixed rate of 40 beats per minute S indicates the point of stimulus C_P is the single fiber membrane action potential which was simultaneously recorded with the isometric tension indicated by M below B) Record taken two minutes after oxygen supply was shut off in the perfusate The rate is the same as in the control record There is alternation in both the membrane action potential and the isometric tension record *(Kleinfeld Stein and Magin [30])*

that can be recorded mechanically this may not be recorded electrically because these portions are not favorably placed for electrocardiographic recording or their effects may be masked by electrical forces in other regions of the heart On the other hand because of the summation of effects in diseased areas no mechanical alternans may be observed yet the position of the damaged muscle may be favorable for electrical recording Kisch[5] has stated that both forms (electrical and mechanical) are indicative of the same mechanism and are brought about by a regular change in the bioenergetic behavior of the heart following muscular contraction He attributes isolated electrical alternans to the electrical activity of the most external portion of the myocardium stating that in the electrocardiogram the portion of the complex from the peak of the R to the end of the T is dependent only or predominantly upon electrical activity in that area of the heart He reasoned that mechanical alternation may not yield an alternation in the electrocardiogram and vice versa Abnormalities restricted to the outer layer of the myocardium sufficient to produce electrical alternation is not always sufficient to make the heart beat or pulse alternate

Although in the great majority of our experiments alternation was observed simultaneously in the single fiber and in the indirect bipolar electrocardiogram 12 per cent showed alternation restricted to the latter (fig 12) This demonstrates that not all fibers participate in the phenomenon If Kisch is correct in limiting the origin of isolated electrical alternans to the most external layer of the heart muscle it may be stated from this experiment that not all fibers in the area probed by the microelectrode necessarily participate in the phenomenon

Our results to date do not permit the presentation of a unified hypothesis to explain the mechanism underlying the various forms of electrical alternation described It is attractive to speculate that changes in magnitude, rate of depolarization rate of repolarization and degree of hyperpolarization of the action potential are on the basis of periodic variations in permeability of the membrane to Na and K ions With regard to Na the changes in magnitude and rate of depolarization of the action potential may be due either to variations in the availability of the carrier substance per se or to variations in the combination of Na and carrier substance (Chapter 2) It is of interest that Eyring and Dougherty[37] have recently suggested the existence of more than one carrier substance for sodium and other ions They stated that With modified membranes and carrier substances quite different ions should be pumped and so concentrated inside or outside the cell as the case may be The exact mechanism by which thyroxine and triiodothyronine alter the membrane permeability to these ions is conjectural Their relationship to the release of acetylcholine is obscure



FIG 11 (*above*) Alternation of hyperpolarization of the frog ventricle following the injection of 1.0 mg Triiodothyronine into the left branch of the aorta. Time lines, gains and zero of potential as in figure 9. (Kleinfeld, Stein, and Magin [30])

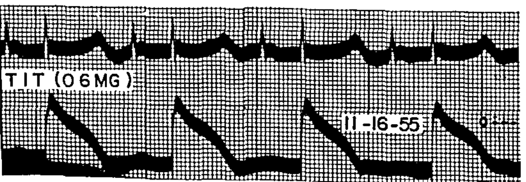


FIG 12 Electrical activity of the frog heart following the injection of 0.6 mg Triiodothyronine into the left branch of the aorta. Procedures same as described in figure 11. Upper record shows alternation of the T wave. Lower record shows normal membrane action potential. The base line shows undulations which have no consistent form and are probably due to movement of the preparation. (Kleinfeld, Stein, and Magin [8])

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circumstances provided the medium is extensive and homogeneous[1] the effects of the dipole or double electric layer on an electrode or point in the medium may be analyzed by the formulae and diagrams in figure 1. From the upper formula and diagram it is clear that the potential (or size of the deflection in the finished record) will be larger the closer the dipole is to the point of recording (the shorter the distance R). Also an elementary knowledge of trigonometry will make it obvious that as the angle θ approaches 0 degrees in the usual mathematical convention the effect on the electrode E in the conducting medium will be maximum and positive. At 180 degrees it will be maximum and negative. In the lower part of the figure the effect of the charged membrane or double electric layer on elec

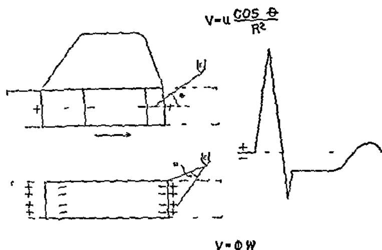


FIG. 1. Methods of analyzing the effect of the membrane action potential on a unipolar lead in a homogeneous conducting medium. The cell is shown diagrammatically twice with the source of electrical energy in depolarization (AB) and repolarization (CD) being regarded as a dipole in the upper figure and as a charged surface or lamina (double electric layer) in the lower figure. In the former the potential of the electrode E is defined by the upper formula in which μ is a constant which depends on the distance between the dipoles and the quantity of charge they carry. R is the distance from the center of the dipole to the electrode E and θ is the angle between R and the positive side of the axis. In the latter the potential V of the electrode E is defined by the lower formula in which φ is a value which depends on the density of the charges on the membrane and ω is a solid angle subtended on a sphere of unit radius about E. Polarity of the electrode is determined by the side of the charged membrane seen by an observer stationed at E.

On the upper cell is drawn the membrane action potential with omission of the overshoot. The diagrammatic electrogram on the right is the record obtained by the electrode in the conducting medium as a result of the changes in the electric field of the medium brought about by the membrane action potential. (From Kossmann, Bull. New York Acad. Med.[2])

PART II CONDUCTING MEDIUM, ELECTRIC FIELD OF THE HEART, LEADS

4 Transformation of the Monophasic Action Potential to the Multiphasic Record, Axial Current and Membrane Current

CHARLES E KOSSMANN, M D

IN PART I, the source of cardiac potential was considered in detail The monophasic record though consisting of recognizable subdivisions, was relatively simple in form The problem to be considered now is how does the monophasic action potential of a single cell or an aggregate of cells acquire the multiphasic configuration so well known to the clinician

To deal with this problem, it is necessary to consider the second determinant of form of the electrocardiogram mentioned in Chapter 1, namely the external conducting medium Specifically, the problem reduces to a consideration of the laws which govern the behavior of electric currents in volume conductors These laws and their application to electrocardiography are not new [1] They are reviewed briefly at this time simply for the purpose of maintaining continuity between data presented in Part I on the source of potential and subsequent material to be presented on electric fields and body surface potentials For purposes of simplicity initial considerations will be confined to a large symmetrical medium with a centric source of potential Failure of the heart in the human torso to meet these requirements is obvious, the significance of this fact will be elaborated in Chapter 5

The monophasic curve is altered when the electrode used to record it is moved to the exterior of the cell and is separated from it by part of the physiologic conducting medium [2] Analysis of the effects are possible because the accession process or period of increasing activity of the cell behaves as though it were a dipole or double electric layer with the positive pole or side facing the direction of excitation of the muscle This results from the fact that with activity as already shown, the polarity of the cell membrane decreases Another way of saying this is that the density of charges on it is decreased The resting muscle just ahead of the active muscle being more densely polarized behaves as though it were positive electrically with respect to the active portion The regression process or period of decreasing activity may be regarded similarly but with the polarity reversed, since the active muscle precedes the resting muscle Under such

the subendocardial regions[4] The e differences in duration of the excited tate are accurately mea ured by the area of QRST, which when reduced to an octantal vector indicates the direction and magnitude of the e differ ences in space Its direction is from an area where recovery is longest to an area where it is shortest It is known as the ventricular gradient[5]

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trode E will be greater as the area of the membrane is larger, and the distance between it and the electrode is smaller. These two variables are measured by the angle ω which is a solid angle subtended on a sphere of unit radius drawn about the point (E in figure) in the conducting medium being studied. The value, ϕ, is determined by the number and the magnitude of the charges on the membrane.

With either of these methods of analysis then, the simple intracellular monophasic curve is converted into a more complicated extracellular, *quadriphasic curve, as shown in figure 1, where accession and regression* are regarded as dipoles (upper figure) or double electric layers (lower figure). The asymmetry of the accession deflections (QRS) and the regression deflections (S T and T), as shown in the figure is attributable to the special circumstance that the electrode in this instance is placed at the distal end of the strip. These two sets of deflections would be symmetrical if the lead was made from the middle of the strip.[3]

The record just described is really the result of current flow across the membrane and the establishment of a symmetric electric field in the extensive surrounding medium. It is accordingly called the "membrane current." If the medium were limited to a thin film about the cell and leading to a recording device were done with two electrodes some distance apart, the resulting trace would be a composite of two monophasic action potentials *in opposite directions slightly out of phase. A similar record* would be obtained if both electrodes were microelectrodes within the cell or if the electrodes were placed at the ends of the cell. In all three circumstances a biphasic record of the "axial current" would be obtained.

Reference to figure 5 in Chapter 1 will disclose that the heart in the frog was so oriented with respect to the forelegs that lead I yielded a biphasic record (upside down). A lead from the epicardium yielded a quadriphasic record with some displacement of the S T segment probably due to excitation block. In a gross way the biphasic trace is in form a first derivative (di/dt) of the monophasic action potential and the quadriphasic record *is the second derivative* (d^2i/dt^2). Mathematical relationships of this kind have been demonstrated to be quite exact in the giant axon of the squid.[4]

In a lead from the medium surrounding the isolated strip of muscle the processes of accession and of regression are equivalent. Although the latter process takes longer the voltages involved are less and the product of the two (time × voltage) is identical with, though opposite in sign, to a similar product for accession. This is the same as saying that the area of QRS is equal to the area of the T wave and *that the sum of the two is zero. In the* electrocardiogram of the normal human ventricle the area of QRST is not equal to zero because certain variables are operative which delay the regres*sion process* in various regions of the ventricular muscle, more particularly

the subendocardial regions [6] These differences in duration of the excited state are accurately measured by the area of QRST, which when reduced to an octantal vector indicates the direction and magnitude of these differences in space Its direction is from an area where recovery is longest to an area where it is shortest It is known as the ventricular gradient [5]

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Einthoven regarded the body as a homogeneous plate. In this medium he elected for leads the right arm, the left arm and the left leg, assuming that these points defined an equilateral triangle. Simple inspection of almost any human body shows that this is not true, and Einthoven knew *it was not true*, but the simplification greatly implemented the understanding and advance of clinical electrocardiography.

Einthoven also assumed that the electromotive force produced by the heart behaved as though it were a dipole and that it was located at the center of and in the plane of the equilateral triangle. This made it possible to establish certain relationships between leads based on an assumed geometry of the body, and Dieuaide[5] designed a rectangular coordinate chart by means of which not only the direction but the magnitude of the vector in the frontal plane could be determined if any two of the three bipolar extremity leads were available. For the purpose of visualizing certain three dimensional problems to be considered later, the triangle for the moment may be assumed to be inscribed in a circular frontal lamina[6] in which the medians of the triangle become radii of the circle (fig. 2).

To put this in clinical language, AO may be regarded as lead I_R, Aa as lead aI_R[7] and lead Aa as a bipolar lead from the surface of the body *in* which *a* is diametrically opposite to the right arm A. In figure 2 it can be seen that AO Aa Aa as 1.0 1.5 2.0. The records obtained should be similar in form but different in magnitude (fig. 3). It is a bipolar method of obtaining the form of lead I_R. A means of doing this clinically has been described[8] and the extremity leads thus obtained are designated II_R, II_L and II_F (figs. 3 and 4). Such leads are a record of approximate "mirror images" (vide infra) and, from the assumed relationships shown in figure 2, are twice the magnitude of a unipolar extremity lead.

The above considerations are based on the statement by Einthoven[2] that the "heart lies as a *material point* in a homogeneous mass and that the distances of the heart from the three leads and also the resistances concerned are equally great." These assumptions were made for practical purposes and there can be no doubt that they have made it possible for

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cate *components in the three axes* (*x* transverse, *y* longitudinal, *z* sagittal) or in the planes (*xz* transverse, *zy* sagittal) other than the frontal (*xy*).

To overcome these limitations, it is suggested that the spatial *instantaneous* manifest axes simply be indicated by $\bar{E}$ or $\vec{E}$, the spatial *mean* manifest axes by $\bar{I}$ or $\vec{I}$, and (for completeness' sake) the spatial *manifest* area of vectorcardiographic loops by L. As in the past, a subscript will indicate the deflection under consideration (e.g., E_R, I_{QRS}) but the axial or planar projection of the vector is to be indicated by an appropriate superscript. For example, F_S is the transverse component (a scalar quantity) of the instant*aneous spatial* vector responsible for the S wave. I^{zy}_{QRS} is the projection of the mean manifest *spatial* axis of QRS on the sagittal plane. L_P is the frontal projection of the manifest area of the spatial loop of the P wave.

5 Heart Vector, Lead Vector, Image Space, Lead Field, Vector Electrocardiography

CHARLES E KOSSMANN, M D

The Heart Vector

The heart vector may be defined as a manifest potential difference in the medium surrounding the heart resulting from its electrical activity Actually, it is the vectorial notation for the equivalent heart dipole,* with a direction parallel to the axis of the poles, a length proportional to the electrical moment (strength), and a sense (head positive, tail negative) depending on the orientation of the poles It is also the vectorial notation for a charged lamina or double electric layer, with a direction normal (perpendicular) to the plane of the lamina and a magnitude and sense determined by the size, density, and orientation of the laminal charges (Chapter 4)

As ordinarily used, it represents an electromotive force in three dimensional space It is a manifest quantity and really a mathematical fiction because its true generator value cannot be determined directly at present, although it can be estimated with the aid of a model of any given subject[1] The *mean manifest potential difference* of Einthoven Fahr, and de Waart,[2] ordinarily designated L differs from it in being two dimensional (frontal plane or E^{xy}) In the light of newer considerations, a less restrictive definition of L seems desirable Clearly different electromotive forces exist instantaneously and on the average during excitation and recovery of either atrial or ventricular muscle The term heart vector, can apply to any of these and to components along any axis or in any plane of the body (fig 1) Most often, it refers to the manifest electromotive force of the ventricles in space †

* In Chapter 4 it was shown that when myocardium enters upon or recedes from the excited state the interface between the active and inactive (resting) muscle behaves as though it were a dipole A mathematical dipole consists of two opposite but equal charges with an infinitesimal distance between them Under experimental conditions it is usual to deal with a finite dipole[1] having a small fixed distance between the poles In any analytical treatment of electric field problems this distance must be considered It is part of the constant μ which in Chapter 4 was used in the formula to define the potential of a point in an infinite homogeneous conducting medium

† With increasing interest in orthogonal or rectilinear components of the electrocardiogram and vectorcardiogram it has seemed desirable to expand and modify somewhat the method of notation suggested by Bayley With that notation it has been possible to indicate in the frontal plane and in three dimensional space manifest instantaneous vectors ($\hat{E}$ $S\hat{E}$) and manifest mean axes ($\hat{A}_P$ $\hat{A}_{QRS}$ $\hat{A}_T$ $\hat{A}_{QRST}$ or $\hat{G}$ $S\hat{A}_P$ $S\hat{A}_{QRS}$ $S\hat{A}_T$ $S\hat{A}_{QRST}$ or $S\hat{G}$) There is no way with this notation to indi

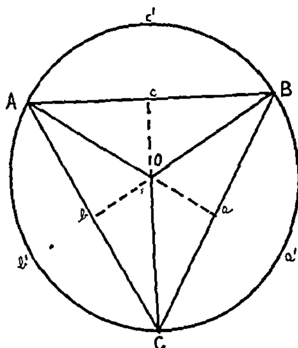


FIG A diagram to illustrate certain geometric relationships of three surface leads (A B C) assuming the source of potential as being at the center of a circular plane lamina The size of the deflections in a unipolar lead from A (comparable to lead V_R) may be visualized as proportional to the length of the line AO Similarly an augmented lead from this point (lead aV_R) will be proportional to the length of the line A_a and a bipolar lead from A and a (lead W_R) proportional to the length of the line Aa joining them On inspection it can be seen that AO Aa Aa as 1 0 1 5 2 0 Similar proportions exist between the various leads from the surface points B and C and the lengths of the subdivisions of the lines Bb and Cc respectively

the young plant electrocardiography ' to bear an amazingly large amount of fruit in accordance with his expectations [9]

The assumptions (Einthoven's hypothesis) may be restated as follows (1) the body is a large conducting medium (2) the medium is homogeneous and resistive (3) the source of potential is a dipole (4) the dipole is at the center of the medium (5) the dipole undergoes no change in position during the cardiac cycle

The Lead Vector and Image Space

Burger and van Milaan [10] in an effort to free clinical electrocardiography from some of these restrictive assumptions particularly numbers 1 2 and 4 above introduced in 1946 the concept of the lead vector and the 'image

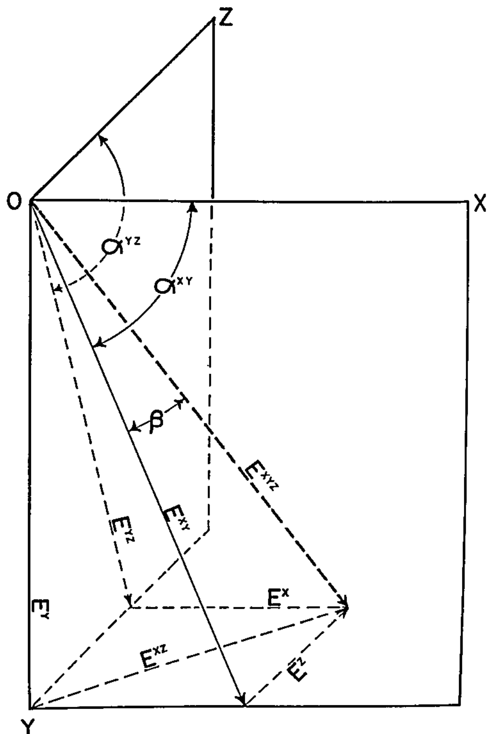


FIG 1 A diagram to illustrate the axial (E E^y E) and planar (E^y E F) components of an instantaneous spatial electromotive force E (or simply Ī) Three angles are also shown which are of u e in orienting an electromotive force α^y the angle between the x axis and the frontal planar projection L^y (Einthoven s angle α) α^y the angle between the z axis and the sagittal planar projection Γ^y β the angle between the spatial vector L^y and its frontal projection I^y

hence are regarded as unity Expressions for e_1, e_2 and e_3 are only in terms of the heart vector F and the effect its angulation with the respective lead has on the recorded potential

Let us suppose on the other hand that the source of current is eccentric with respect to points R L and F so that it is closer to L than to R Under the circumstances the scalar magnitude of lead LF will be larger than of RF (Chapter 4) This difference can be illustrated geometrically by lengthening lead LF in the triangle which then becomes scalene in form (fig 5B) It can be seen at a glance that the projection of F on the leads will not be the same as in the equilateral triangle not only by virtue of the different

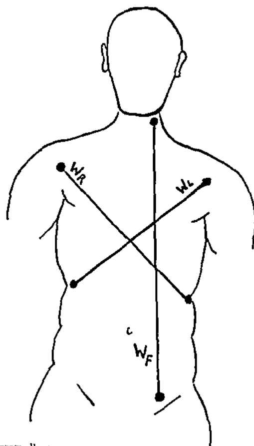


FIG 4 Diagram illustrating the bipolar method of obtaining extremity potentials The second electrode is placed diametrically opposite to the extremity being studied and in each instance yields an approximate mirror image of the potential of the latter Hence the bipolar leads W_R W_L and W_F have an approximate value of twice the unipolar leads V_R V_L and V_F

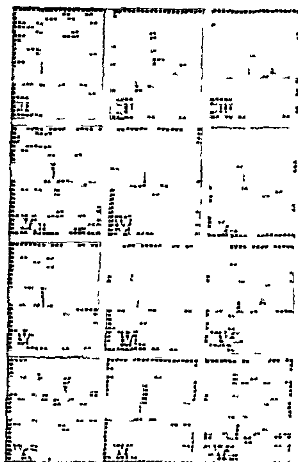


FIG 3 Bipolar extremity lead (I II III) extremity potentials (V_R V_L V_F) augmented extremity potentials (aV_R aV_L aV_F) and bipolar extremity potentials (W_R W_L W_F) in a patient with arteriosclerotic heart disease To be noted is that *the magnitude of the deflections in the augmented extremity potentials is 1 5 times* the magnitude in the extremity potentials but in the bipolar extremity potentials the value is somewhat greater than 2 0 This is in contrast to the prediction in figure 2 (From Kossmann Bull New York Acad Med [6])

space ' Explanation of these can be most easily approached by way of the equilateral triangle Using Einthoven's formulations[3] and notations it is clear in figure 5A that e_1 the projection of E on lead RL has the value $e_1 = E \cos \alpha$, and that when E is horizontal $e_1 = E$ and when E is vertical $e_1 = 0$ The expressions for e_2 and e_3 are derived in the well known geometric manner and are $E \cos (\alpha - 60°)$ and $E \cos (120° - \alpha)$ respectively

Of significance is that the assumption of a symmetrical field and equidistant lead points (equal sides of the triangle) do not make it necessary to use any factor ' which is needed in a distorted field The leads (*RL RF LF*), being equal in length, are affected by the heart vector similarly and

Clearly if the principles above apply to bipolar leads they al o apply to unipolar leads which are really bipolar leads with one pole at zero potential The expre ion above then becomes u ing Frank s notation[1] a dot product* of two vectors

$$V = \bar{C}\,\bar{P} \qquad (2)$$

in which V is the symbol for potential, $\bar{C}$ the correction coefficient or lead vector and $\bar{P}$ the projection of the heart vector on the lead vector

Since two vectors are involved and each may be broken down into its orthogonal components (fig 1) in accordance with the law of superpo ition[13] for a linear medium the equation becomes

$$V = \bar{C}\,\bar{P} = c_x p_x + c_y p_y + c_z p_z \qquad (3)$$

in which c_x c_y c_z and p_x p_y and p_z are the three calar components of the vectors C and P re pectively For any given electrode po ition c_x c_y and c_z are constant and depend on uch determinants as the size hape and characteristics of the medium and the location of the current ource of potential[1]

The lead defined the investigator is in a position to determine the correction coefficients Once determined they can be used to obtain the correct orthogonal components of the heart vector and record thereby electrocardiograms or vectorcardiogram undistorted by the effects of an irregular body surface inhomogeneities or an eccentric source of the current Unfortunately this cannot be done directly with any degree of accuracy in living man although we have developed a technique of reciprocal stimulation of a tridimensional electrode which shows promi e[11] It can and has been done on model by Burger and van Milaan[10] by Frank[15] and by Schmitt[25] The unipolar technique used by Frank is described for the sake of implicity

In the formula $V = C\,P$ any two values must be known in order to get the third In experiments on a model a dipole of constant moment is used which then can be regarded as unity In order to get the values of c_x c_y and c_z for any surface lead the dipole at the electrical center is oriented along the assumed orthogonal body axes in turn the values of the other two thereby become zero (ee equation 3 above) From the x y and z values of C the locus of the lead vector can be obtained and plotted in pace a has been done by Frank[15] The image surface which is defined by the loci of the lead vectors of innumerable surface leads differs very considerably from the anatomic surface of the body (ee ref 15 Figs 1 2A, 2B and 2C) The electrical configuration of the human thorax bulges promi

* The product of a vector and the projection of another vector upon it is u ed in many cientific fields e pecially astronomy and is known as a dot product

angulations between the two but also because the different rather than equal distances between lead points result in different "weights"[11] of the three leads. Each lead, with direction and length, meets the requirements for a vectorial quantity, the lead vector (also called image vector, coefficient of correction, transfer function, transfer impedance). Further, it is apparent that in leading from such an asymmetrical field, these factors of length and direction of the lead cannot be ignored.

To return to the problem of the value of e_1 in the scalene triangle, it now becomes

$$e_1 = RL \cdot E \cos \alpha \tag{1}$$

(analogous to the relation Work = Displacement × Force × cos α) in which e_1 is the scalar value of the lead (potential difference), RL is the lead vector, and $E \cos \alpha$ is the heart vector projected on the lead, RL.

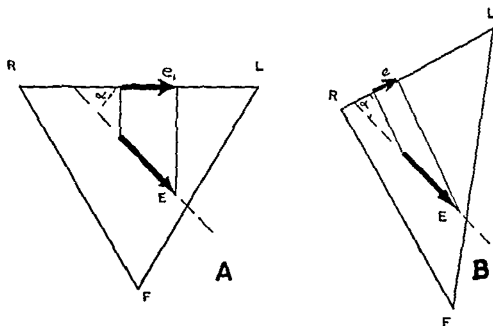


Fig. 5. A diagram to illustrate the different significance of leads in an equilateral triangle (A) and a scalene triangle (B). In the former the leads RL, RF and LF are equal in length. They may be regarded as units, and thus the projection of the instantaneous electromotive force E on a lead (e_1 on lead I in the figure) is determined only by the cosine of the angle alpha. In the latter the point source of potential is eccentric, and the scalar value of any point in the medium will be determined by its nearness to this point source. In B it was assumed to be nearer to L than to R; hence L is represented as being *farther* from the source, and LF becomes longer than RF. In such a triangle the unequal distances of the lead points from the source can be corrected by a coefficient which depends on the length of the lead (the lead vector).

garded as a generalization of the Einthoven equilateral triangle. It usually has an asymmetrical scalene appearance, with lead III larger than lead II, but this varies depending on the location of the heart or dipole center assumed by the investigator.

If one accepts the orthogonal correction coefficients of Burger and Frank, determined from different models but remarkably alike in magnitude, then the heart vector can be calculated by a triangular coordinate system as in the Einthoven triangle, but the density of units of measurement must be porportional to the length of the sides of the Burger triangle[11] (fig. 6). From the medians of such a triangle, another can be constructed for determining the heart vector from the augmented extremity potentials. A combination of the two triangles into a hexaxial reference system can also be made (fig. 7).

Implicit in such calculations is that the source of potential in the heart can be regarded as an equivalent fixed position dipole. There is evidence both for and against the dipole assumption. Some of our experiments[6, 17]

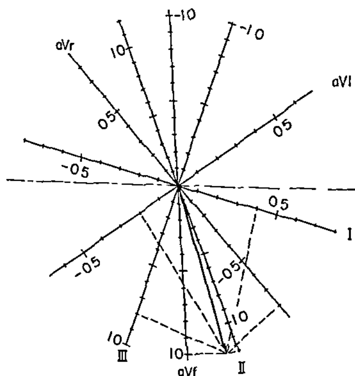


Fig. 7. Hexaxial reference system constructed from the sides of the two triangles in figure 6 (Brody)

nently to the left and forward by virtue of the location of the "heart center" in the left anterior quadrant of a transverse section of the thorax at the heart's level

Important by products of the study with the particular heart center selected by Frank[15] were that Einthoven's triangle is not equilateral but scalene, with lead III the longest and lead I the shortest side, that the plane of the triangle does not pass through the heart center but behind it, with its cephalic end farther posterior than its caudal end that the central terminal of Wilson, Macleod, and Barker is not at zero potential, and that the "equilateral" tetrahedron does not include this specific heart center within its borders

The Burger Triangle

If the lead vectors for the bipolar extremity leads are determined as described above or in other ways, either in models or in man [15] [16] and arranged as a triangle the latter is called the Burger triangle It may be re

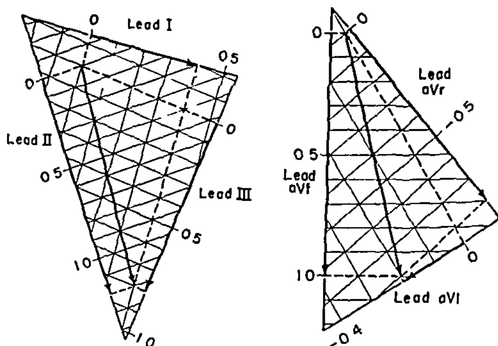


Fig 6 Transformation of a Burger triangle (left) into a triangular coordinate plot The density of scale marks per unit length is proportional to the length of each side (in this instance I III II as 4 5 6) Projections of the electrical axis on each side of the triangle indicate the magnitudes of lead I II and III

On the right is a scalene triangle constructed from the medians of the preceding figure Spacing in the leads is determined by the same principle employed in the figure on the left Projections of the electrical axis on the sides of the triangle indicate the magnitudes of leads aV_R aV_L and aV_F (From Brody Am Heart J [11])

Substituting the vector $\mathbf{J}$ for $\mathbf{i}$ they obtained the equation

$$i = \mathbf{J} \cdot \mathbf{e} = J_x e_x + J_y e_y + J_z e_z \qquad (5)$$

which is not unlike Frank's equation given above. In fact, it states that the current field $\mathbf{J}$ at any point in the heart resulting from the introduction of a unit current into the lead has the same direction and intensity as the lead vector at that point.

Determination of lead fields in three dimensions has offered even greater practical difficulties than the determination of lead vectors. As a result the synthesis of leads based on the analysis of lead fields has not progressed to any great degree at the clinical level. Further, if the lead field differs from point to point in the heart, an argument used to defend the nondipolar nature of the heart's current source, it is visualized that practical use of it can only be made by integration (which yields the lead vector) or by partial spatial differentiation of lead vectors in models and synthesis of composite leads to yield the desired components[30-35] (see Chapter 6).

Vector Electrocardiography

The above considerations of the heart vector make it obvious that information obtained by synthesis of a single vector from the usually recorded scalar leads can be only a first order approximation of the truth, however valuable it may be otherwise.

Actually Ashman[4] first called attention to the spatial vector method in one of his papers on the ventricular gradient. Grant[5, 6] saw the possibilities of the method based on perpendicular plane projection. The assumption made was that electrically the heart may be treated as an equivalent dipole. The axis of the dipole is a flow line perpendicular to it and passing exactly between the poles is an isopotential line of theoretically zero potential. By extending this presumed straight line out to the surfaces of the presumed cylindrical body and regarding it as defining a plane perpendicular to the axis of the dipole, the body is divided into two parts, one of which is electropositive and the other electronegative in the current field of the dipole. By observing in a variety of surface leads the simultaneous deflections in either direction from the baseline, the perpendicular plane can be defined in the body. The procedure has come to be known as spatial vector electrocardiography (Grant).

The method has limitations which may be listed as follows: (1) the heart vector calculation is based on the concept of the infinite or large homogeneous conducting medium; (2) in certain pathologic states and even in normal subjects the plane is not a flat surface[7] (fig. 8); (3) in the method the body is assumed to be a cylinder; a centric dipole in a cylindrical bounded field yields a surface isopotential which is S shaped[8] (fig. 9).

with intracardiac leads favor the concept. In one patient studied, four out of five recognizable deflections in simultaneously recorded intracardiac and precordial leads could be ascribed to a single current source. Schmitt,[18] and later Frank,[19] by demonstrating exact mirror images (figs. 3 and 4) on opposite sides of the body for all surface points ("cancellation potentials"), have given support to the concept. Analyses by McFee and Johnston[20] and by Hartmann and associates[21] and certain occasional clinical observations in an isolated chest lead suggest, on the other hand, that proximity to the source of potential, even with the thorax intact, may determine a local (nondipolar or multidipolar) effect on the exploring electrode.[11]

To be emphasized, too, is the assumption in the Burger concept of a fixed position of the dipole. If this is not true, mathematical treatment of a variety of field problems becomes exceedingly complex and clinical solution an almost insurmountable problem. There is some evidence that the position of the dipole does in truth vary.[22]

The Lead Field

McFee and Johnston[20] have pointed out that the lead vector concept requires the retention of one of Einthoven's postulates, the validity of which is questioned by many. This is the assumption that the electromotive force of the heart may be regarded as a dipole of variable moment. To overcome this restriction, they have developed the concept of the "lead field," which may be regarded as a generalization of the lead vector concept.

By definition, the "lead field" is a field of current produced in the body when a unit current enters the negative terminal of a lead and leaves its positive terminal. Such a current field will have a certain intensity and direction at every point in the body and in the heart. Hence, at each point the current can also be regarded as a vector $\bar{J}$.*

McFee and Johnston, in accordance with Helmholtz' reciprocity theorem,[13] have deduced that every element of an electromotive surface within the heart will produce an open circuit voltage v in a given lead equal to the potential difference e of this element multiplied by the current i which passes through it as a result of connecting the lead to a unit source of current. Simply stated,

$$v = ei \qquad (4)$$

* In an electric field two vector quantities are defined: F, the intensity, and D, the flux density. F is measured in dynes/statcoulomb and is the reverse or negative vector of potential gradient (P. G.) measured in statvolts/cm. The electric flux density is further defined as $D = kF$ (lines of flux/cm²). Hence, it differs from field intensity only in magnitude determined by the dielectric constant k of the medium.[23] In a reciprocal field, F corresponds best to J above. Further, P.G., with the sign changed,[24] is identical. All three in a given reciprocal field define the lead vector at any specific point in that field.

leid are lost Grant was quite aware of this and his sugge ted studies of the 0 04 vector' (approximately Q) and the terminal vector (S wave)

In the method the relation of the QRS and T vectors in space defined by the size of the angle between the two can be calculated as follows [6] but the accuracy of the calculation can be no more accurate than the determination of the vectors The three extremities u ed for the frontal triangle and a point on the back are as umed to be equidistant from the source of potential in the center of the frontal triangle Under such circum tances an isosceles tetrahedron is formed If in addition the axial components are as umed to be lead I = x a vertical median perpendicular to lead I = y and a line joining the center of the frontal triangle with the point on the back = z then the magnitude of any vector in space will be defined by the square root of the um of the quares as

$$E = \sqrt{x^2 + y + z} \qquad (6)$$

To calculate the angle θ between the spatial mean manife t potential of QPS and T the following equation could be u ed

$$\cos \theta = \frac{(A_{QRS} \times A_T) + (A^y_{QRS} \times A^y_T) + (A_{QRS} \times A_T)}{A_{QRS} \times A_T} \qquad (7)$$

in which A_{QRS} and A_T are the respective magnitudes of the mean manifest spatial vectors of QRS and T and the values in the numerator are the projections of these on the assumed indicated rectilinear coordinate

In the method the frontal plane vectors are determined as described earlier the sagittal plane vectors are determined from the y component and lead BF (back to left leg) a lead assumed to make an angle of 45° with the

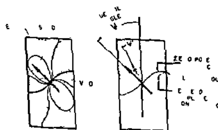


FIG 9 Current lines (dashed) and isopotentials are shown at the left in cro s section for a homogeneous conducting cylinder in which is immersed a centric current dipole The i opotential surface V = O which is not a plane surface is seen to meet the cylinder wall at right angles as do all other boundary isopotentials The error entailed in the perpendicular plane construction is indicated on the right which is drawn approxima ely to scale The angles ψ and ψ are the true tilt of the dipole and the apparent tilt obtained by perpendicular plane construction respectively (From Frank and Kay Circulation)

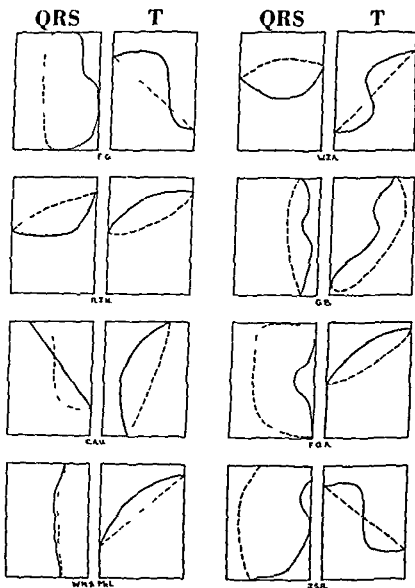


Fig 8 Diagram to illustrate minor and moderate deviations of the null contour from the usual ellipse in 8 subjects The thorax is represented as a cylinder Approximately 25 per cent of normal subjects will show such deviations (From Langner Dewees and Moore Am Heart J [27])

If the angle of the true heart vector is compared to the apparent angle they are found to bear a ratio of 1 6 to 1 0 to each other provided the maximum degree of tilt from the cylinder axis is less than 45° If the dipole is assumed to be eccentric the problem becomes complicated beyond calculation, (4) if a mean manifest potential is determined the early and late vectors, so important diagnostically as the Q wave and the S wave in scalar

leads are lo t Grant was quite aware of this and has suggested studies of the 0 04 vector (approximately Q) and the terminal vector (S wave)

In the method the relation of the QRS and T vectors in space defined by the size of the angle between the two can be calculated as follows,[38] but the accuracy of the calculation can be no more accurate than the determination of the vectors The three extremities used for the frontal triangle and a point on the back are assumed to be equidistant from the source of potential in the center of the frontal triangle Under such circumstances an isosceles tetrahedron is formed If in addition the axial components are assumed to be lead I = x a vertical median perpendicular to lead I = y and a line joining the center of the frontal triangle with the point on the back = z then the magnitude of any vector in space will be defined by the square root of the sum of the squares as

$$E = \sqrt{x^2 + y^2 + z^2} \qquad (6)$$

To calculate the angle θ between the spatial mean manifest potential of QRS and T the following equation could be used

$$\cos \theta = \frac{(A_{QRS} \times A_T) + (A'_{QRS} \times A'_T) + (A''_{QRS} \times A''_T)}{A_{QRS} \times A_T} \qquad (7)$$

in which A_{QRS} and A_T are the respective magnitudes of the mean manifest potential vectors of QRS and T and the values in the *numerator* are the projection of these on the assumed indicated rectilinear coordinates

In the method the frontal plane vectors are determined as described earlier, the sagittal plane vectors are determined from the *y* component and lead BF (back to left leg) a lead assumed to make an angle of 45° with the

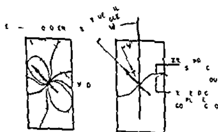


FIG 9 Current lines (dashed) and isopotentials are shown at the left in cross section for a homogeneous conducting cylinder in which is immersed a centric current dipole The isopotential surface V = O which is not a plane surface is seen to meet the cylinder wall at right angles as do all other boundary isopotentials The error entailed in the perpendicular plane construction is indicated on the right which is drawn approximately to scale The angles ψ and ψ' are the true tilt of the dipole and the apparent tilt obtained by perpendicular plane construction respectively (From F an and Kay Circulation [9])

frontal vertical median To be exactly comparable to frontal leads this lead should be corrected by the factor $\sqrt{1.5}$

In practice, the spatial angle can most easily be determined by a variety of devices [9, 30, 31] or with the aid of tables [32] Although the maximum normal value originally given was 50° later observations indicate that the 95% range is probably in the neighborhood of 7° to 90° in middle aged men and greater in overweight subjects [33]

In conclusion, it may be said that vector electrocardiography as a clinical method is interesting and useful but, being a generalization of the scalar method, tends to obscure some of the details of clinical value revealed by the latter method Whether the application of the image space concept to the method will increase its precision can only be decided in the future One study [34] thus far has demonstrated surprisingly little effect of an orthogonalized axis system on the variability of the QRS and T vectors and the angle between them when compared with the results of an equilateral tetrahedral reference frame

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6 Vectorcardiographic Leads and Reference Frames, Differential and Universal Vectorcardiography

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THE INITIAL endeavor to record the electrocardiogram as a vector time trace directly was made by Mann in 1920 with the design of his monocardiograph. His work was not published, however, until 1938.[1] He used lead I as the x axis and the average of leads II and III for the y axis to record a monocardiogram in the frontal (xy) plane. Since then a variety of methods of leading or reference frames has been designed,* each purporting to yield more or less accurately the correct axial components (x, y, z) and hence the true planar (xy, xz, zy) configurations of the vectorcardiogram. Assuming certain geometric relationships between the electric heart center and surface leads, later authors[3, 4, 5, 6] have introduced *normalization factors* in order to make the components yielded by the leads in any one system comparable in magnitude to each other. Despite such corrections, it is clear from what was presented in Chapter 5 on the image space that electrical computations based on the *geometry* of the body may be quite erroneous.

Most recent progress in vectorcardiography, therefore, has been centered around the design of an "orthogonalized" system of three-dimensional leading which will yield as accurately as possible the true rectilinear components of the electrical record free of the distortion caused by irregularity of the body surface, inhomogeneity of the surrounding medium, and eccentricity of the heart.

In any three dimensional system used, it is obvious that a minimum of four electrodes must be attached to the body. Burger and his associates[7] have designed two 4-electrode frames of reference designated the B_1 and the B_2 systems (fig. 1), which are modifications of the equilateral tetrahedron. In the B_1 system the first three electrodes are attached to the extremities as in Einthoven's triangle; the fourth is placed high on the sternum at the level of the axillae. In the B_2 system, the left leg is used as one attachment; the other three are high on the thorax, also at the level of the axillae. One of the latter, S, is on the back over the vertebral column; the other two, P_6 and L_1, are on the front, midway between the midline and the anterior axillary fold on each side (approximately the midclavicular line). From the data available on the lead vectors of a scaled-down human model

* See Chapter II of the book by Grishman and Scherlis[2] for descriptions of earlier methods.

studied by Burger and van Milaan,[8] the axial components of each lead system can be derived from the three bipolar leads when the right arm (R) or the right side of the chest (R_b) is used as the common electrode (see formula below) By a somewhat subjective method of comparison, these investigators found their systems to yield better corresponding results with each other than either did with the equilateral tetrahedron of Wilson, Johnston, and Kossmann[4] Because, with proper factoring the agreement of the last frame called W_4, with B_1 was better than with R , at a later date the correction coefficients were determined for the W_4 system[9] to make correspondence with B_1 more exact The corrected W_4 frame was designated W_4''

McFee and Johnston[10] suggested a variety of ways of creating lead systems, making use of the lead field principle (Chapter 5) but provided no data for a definitive reference frame in man The methods suggested for designing leads were "synthesis by combination" (essentially a normalization of scalene configurations by appropriate resistor networks) and "synthesis by adjustment of the lead field current at the body surface" Later, the Ann Arbor group[11] applied the principle to the design of a multielectrode grid for recording the sagittal component of the heart vector

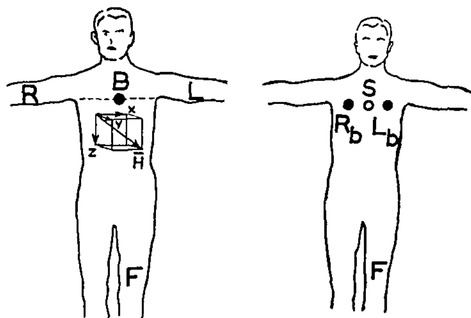


FIG 1 Positions of the electrodes in the B_1 (left) and R_2 (right) system of Burger and his associates R L and F are the extremities B is the electrode on the sternum S is the electrode on the back In the figure on the left the x and z components of the heart vector H are interchanged compared to more recent custom (From Burger van Milaan and Den Boer Brit Heart J 7)

It has been pointed out [9] that the central terminal of Wilson, Macleod and Barker has certain attributes which may be useful in vectorcardiography. Pairing the terminal with the left leg on the image surface of Frank's homogeneous torso yielded a lead roughly parallel to the y axis and paired with the back electrode a lead which was roughly parallel to the z axis. In the frontal plane the Rl lead was *contaminated* by quantities of the y and z components which tended to balance each other. This resulted in favorable scalar shapes of the components but scale factors still had to be applied. Frank suggested that $V_F - V_C$ be recorded at 0.75 of the usual amplitude of the other two leads ($V_L - V_R$, $V_B - V_C$) of the equilateral tetrahedron. His data suggest that the central terminal may have a place in vectorcardiography for a purpose other than the creation of a nullpotential electrode. Further, *two-dimensional central terminal networks can* be designed[10] for recording the components of the heart vector (*component* terminals).

Schmitt and his associates[12, 13] have published two different reference frames designated SVEC II and SVEC III respectively. SVEC is an abbreviation for *stereovectorelectrocardiography* for the method not only attempts to correct the magnitude and direction of the components of the spatial vector but also to present the ease as a three-dimensional stereoscopic vector trace for visualization or recording. The SVEC III system, which requires the application of 14 electrodes (8 for the sagittal lead, 4 for the transverse lead, and 2 for the vertical lead), 12 resistors, and amplification corrections so that the x component and y component are 75 per cent and 71 per cent of the z component respectively, was determined by experiments on a full scale human model filled with saline. A dipole was placed *ucce* *ively at the center* and at the eight *corners* of a cube 8 cm. in size positioned at the heart center as determined radiographically in the model subject. The lead *vectors* (*tran* fer impedances) for a great many standard leads and surface points were determined with the dipole in each of the nine heart locations by successive orientation of the dipole in the three axes (see Chapter 3). From the *…* the amount of contamination of a lead by other than its dominant *component*, obvious from the tilt or deviation from the assumed true axis, was corrected by partial derivative compensation.* In this way, undesired components and lengths were sys

*For each lead regarded as a possible desirable constituent of a weighted orthogonalized combination, the variations in the lead vector are measured as the heart dipole is made to scan the heart volume of a model in the three primary directions. In a useful lead, one component will dominate, the *other contaminating components* will be small and vary in strength and possibly sign. From several such leads a *composite* lead is eventually found in which the *contaminants* in the constituent leads cancel for all regions of the heart.[12]

tematically balanced out, as suggested by McFee and Johnston.[10] As mentioned in Chapter 5, the lead field generalization of the lead vector concept is not applicable to the heart as a whole, and even McFee and Johnston in designing their leads use the lead field determined at the "center" of the heart. By way of digression, it should be noted that Schmitt's experiments demonstrate also that "local" effects of a dipole do occur if the heart size relative to the body is as assumed in his model.

Frank[14] has devised a system using seven electrodes, with balancing and compensating resistances required for orthogonalization and normalization also determined by means of the partial derivative compensation principle. The x and z components are derived from three and five electrodes respectively (fig 2) placed at the level of the fifth intercostal space at the sternum. The y component is the difference in potential between the right

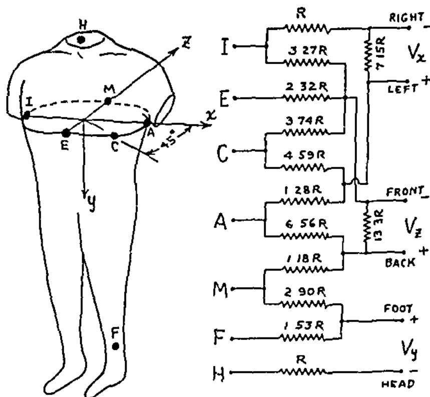


Fig. 2. Frank's system of vectorcardiographic leads. Of the seven electrodes, A, C, I, E and M are located at the same transverse level (approximately the fifth intercostal space). H is on the back of the neck and F is on the left leg. These electrodes may be connected directly to computing and compensating networks (right), the outputs of which are the three potential differences V_x, V_y and V_z, which are proportional to the respective axial components of the dipole with equal standardization factors. (From Frank, Circulation.[14])

side of the back of the neck (H) and a terminal divided between the left leg (F) and a point on the midback (M) also used in the circuit for acquiring the z component Although determined in a model with a single dipole location the system is said to be relatively insensitive to dipole position Frank[15] has also designed an R L F B system with corrections applied by a system of resistors to the lead points as in the W" system (an orthogonalized tetrahedron or average computing system) but has found the lead vectors in it quite sensitive to dipole location

Helm[16] has suggested a frame based on Frank's data by using seven electrodes (and one for ground) Two of these consist of large synthetic sponges ¼" in thickness soaked in sodium chloride solution which in effect are substitutes for small electrode combinations with resistors [11] One is used as the left sided electrode for the transverse lead and is centered approximately on the left anterior axillary line at the level where the fifth intercostal space crosses the parasternal line The other is placed on the front of the chest at the same level to form the anterior terminal of the sagittal lead Other small sized electrodes are placed as shown in figure 3

Comparative Studies of Vectorcardiographic Reference Frames

Comparative studies of many of the common reference frames in use have been made Those by Burger[7, 9] have already been mentioned Milnor Talbot and Newman[17] have compared the Duchosal and Sulzer trihedron [18] the Milovanovitch leads [19] and the equilateral tetrahedron [4] and Frank[20] has compared the first and last of these with the cube of Grishman and Scherlis [2] Since all of these record electrical components based on the geometry of the body and only the tetrahedron utilizes normalizing[4, 5] factors considerable differences in the form of the vectorcardiograms were demonstrated The orthogonalized systems of McFee and Johnston Schmitt Frank and Helm have been compared by Moore and Langner [21] In general these systems compare fairly well and the data suggest that the SVEC III is perhaps the best Frank and Seiden[22] have compared the seven electrode precordial system designed in their laboratory with the R L F B system also designed there They found that the latter yielded quantitatively significant variations in the z and x components in 50 per cent and 20 per cent respectively of normal subjects and patients and, in addition gave practical difficulties from somatic tremors

In attempting to appraise these various reference frames it must be kept in mind that all are based on surface measurements made on a model filled with tap water or saline and with a dipole located in this fluid at one or several presumed electric centers of the heart Only in this laboratory [3] have attempts been made thus far to determine image vectors in living man (Chapter 7)

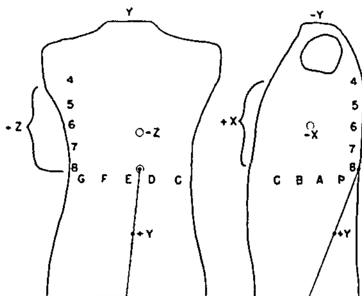


FIG 3 Helm's system of vectorcardiographic leads The columns (letters) and rows (numbers) on the thorax are designated as by Frank The component leads are as follows —x a small limb electrode in the right axilla between H and I at level 6 (approximately midway between the right anterior and midaxillary lines at the level of the fifth intercostal space at the parasternal line) +x a square saline containing sponge centering at the same transverse level and extending from the left mid clavicular to the left posterior axillary line (covering approximately the 20 points I A B C at levels 4 to 8) —z a small limb electrode on the back midway between the vertebral and left scapular lines 1 cm caudad to the level of electrode —x (mid way between M and N at level 6¼) +z a square saline containing sponge centered at the same level as electrode +x and extending from but *not* in contact with the anterior margin of the latter (left midclavicular line) to the right midclavicular line (covering approximately the 25 points C D E F G at levels 4 to 8) —y a limb electrode on the forehead or in the submandibular region +y a network of two electrodes one on the left leg and one on the back at level 8 on the same vertical line as electrode —z (From Helm Am Heart J [16])

The location in the body of the equivalent dipole during activation of the ventricles is the heart center It is probably the most critical of all the determinants of image space, as has been repeatedly emphasized by Frank In some investigations[12, 13] it has been assumed to be at the anatomic center of the ventricles as determined by biplanar x rays of the chest of the model subject It has also been determined electrically by a precision cancellation technique[4] The method is based on the finding in the model that at the transverse level of the equivalent dipole the contribution of the vertical component to surface potentials is small so that equation (3) in Chapter 5 becomes

$$V_T = c\, p_x + c\, p$$

where V_T is a potential at the transverse level of the body or model which includes the heart center[24] To apply the method the cancellation data obtained must be fitted to torso model data, thus far available on only one subject However it appears that image surface at the transverse level of the heart are relatively insensitive to chest contours and body builds and even types of heart disease[25] and such data fitting seems valid (see ref 24 for details and uses of the method)

Somewhat disturbing in an appraisal of recent quantitative approaches to vectorcardiography is the fact that the heart center probably moves during ventricular depolarization especially if there is bundle branch block, and that the center is certainly not the same for atrial activation (P wave) or ventricular recovery (T wave)

Under the circumstances it seems unwise to be dogmatic about the eventual clinical usefulness of the vectorcardiographic method There are ardent defenders of it as well as attackers That it displays minute phase differences better than the scalar record is admitted but this is a minor advantage considering the present difficulties in leading and recording Certain spatial vectorial parameters can be studied relatively easily with the stereovectorelectrocardiogram[1] or panoramic vectorcardiograph[17] which may be helpful in differentiating the normal from the abnormal heart Making certain assumptions the relative electrical work done during excitation and during recovery of the ventricles can be determined from the area of the spatial QRS and T loops[26] but a large scale clinical test of the method must wait upon the construction of an accurate integrator of these spatial areas (Chapter 7)

Judging from a half century of experience with the Einthoven triangle it is very probable that some semi orthogonal system will eventually be adopted for routine clinical use even though it may not meet the rigid requirements of the engineer in every case Ideally the lead vectors should be determined in each patient individually but the likelihood that such a procedure if ever actually worked out will be practical is small The so-called quantitation of electrocardiography therefore is approaching a second order of magnitude but the approach will require compromises with practicality if the method is to continue to maintain its valuable place in clinical cardiology

Differential Vectorcardiography

The processes of excitation and recovery occur independently in the atria and in the ventricles Since as shown earlier each process is accompanied by an electromotive force which varies in magnitude and direction with time each can be recorded as a time vector trace It is possible then to identify Lissajoux figures for P T_P QRS T and U Since normally,

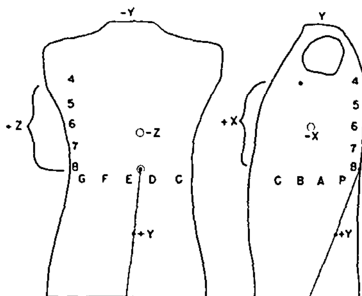


FIG. 3. Helm's system of vectorcardiographic leads. The columns (letters) and rows (numbers) on the thorax are designated as by Frank. The component lead are as follows: −x, a small limb electrode in the right axilla between H and I at level 6 (approximately midway between the right anterior and midaxillary line at the level of the fifth intercostal space at the parasternal line); +x, a square saline-containing sponge centering at the same transverse level and extending from the left midclavicular to the left posterior axillary line (covering approximately the 20 point I, A, B, C at levels 4 to 8); −z, a small limb electrode on the back midway between the vertebral and left scapular lines 1 cm. caudad to the level of electrode −x (midway between M and N at level $6\frac{1}{4}$); +z, a square saline-containing sponge centered at the same level as electrode +x and extending from, but *not* in contact with, the anterior margin of the latter (left midclavicular line) to the right midclavicular line (covering approximately the 25 points C, D, E, F, G at levels 4 to 8); −y, a limb electrode on the forehead or in the submandibular region; +y, a network of two electrodes, one on the left leg and one on the back at level 8 on the same vertical line as electrode −z. (From Helm: Am. Heart J.[16])

The location in the body of the equivalent dipole during activation of the ventricles is the heart center. It is probably the most critical of all the determinants of image space, as has been repeatedly emphasized by Frank. In some investigations,[1, 13] it has been assumed to be at the anatomic center of the ventricles as determined by biplanar x-rays of the chest of the model subject. It has also been determined electrically by a precision cancellation technique.[4] The method is based on the finding in the model that at the transverse level of the equivalent dipole the contribution of the vertical component to surface potentials is small, so that equation (3) in Chapter 5 becomes

$$V_T = c_x p_x + c_z p_z$$

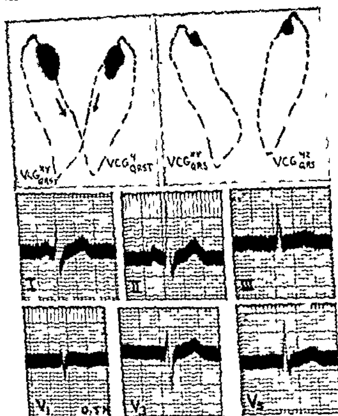


FIG 5 Frontal (VCG^{y}_{QRST}, VCG^{y}_{QRS}) and sagittal (VCG_{QRST}, VCG^{y}_{QRS}) vector cardiograms of a male subject *in the early* twenties The arrows show the *direction* of rotation of the loops *The reference* system used was the *isosceles tetrahedron* and the sagittal records are viewed from the *left* The bipolar extremity leads (I II III) and 3 chest leads (V_1, V_3, V_5) of the same subject are included In addition to showing one form of the normal vector*cardiogram* the figure illustrates differential electrocardiography with the loops *of* QRS and T on the left and only of QRS *on* the right (From Hoffmann *in* Meakins *Practice of Medicine* ed 6 St *Louis* C V Mosby Co 1956 fig 115)

a hold circuit is initiated to inactivate the input until the entire cardiac cycle is completed The leading *edge of the* hold voltage initiates a delay circuit and the trailing edge of the latter voltage trips the exposure voltage The end of the exposure voltage operates the film advance circuit to the camera An example of records made by the instrument are shown in figure 5 Hellerstein and his associates[3] have designed a similar instrument using the initial part of QRS as the triggering voltage and selective blanking and unblanking for recording the desired parts of the vectorcardiogram

these occur sequentially (with some overlap of T_P and QRS), they will tend to superimpose on the persistent screen of the cathode ray oscilloscope.

For a variety of reasons, including the need of a new approach to certain fundamental problems in vectorcardiography,[26] an instrument was designed and constructed to record each of the vectorial forms independently.[7] Since the time relationship of the vector forms of each heartbeat remain relatively fixed, it is desirable to activate all timing circuits of the instrument from within the group. For this purpose, the P wave is used, which limits the method to situations in which this deflection is present. The desired loop or part of a loop is photographed by means of variable hold, delay and exposure circuits incorporated in a synchronized exposure timing unit (fig. 4). A trip voltage is generated by the leading edge of the P wave. Because every other rise in voltage would similarly act as a triggering agent,

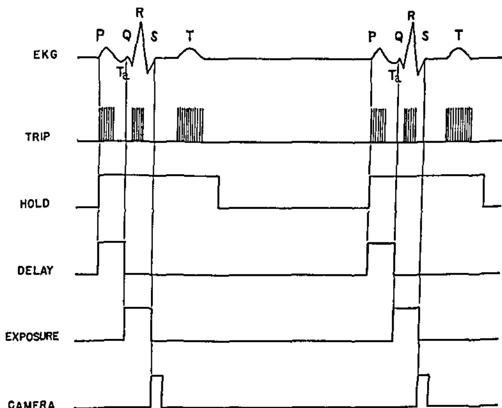


Fig. 4. Diagram illustrating the voltages generated by the synchronized exposure timing unit of the differential vectorcardiograph. The circuits have been adjusted to record the QRS deflections (see fig. 5). All upward electrocardiographic deflections are transformed into a series of pulses by the trip circuit but only the first pulse is used to energize the *hold* and *delay* circuits. *Simultaneous points are indicated* by the vertical lines. (From Briller, Marchand and Kossmann: Rev. Scient. Inst.[17])

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It must be apparent from the formulations given in Chapter 5 that the use of correction coefficients in vectorcardiographic leads involves two mathematical procedures to a lead—multiplication and addition This becomes apparent from the linear equations for the components of the heart vector if the minimum of three bipolar leads (four electrodes on the body) are used (ref 29 and Chapter 7)

$$x = \alpha_1 \text{ (lead)}_1 + \alpha \text{ (lead)} + \alpha_3 \text{ (lead)}_3$$

$$y = \beta_1 \text{ (lead)}_1 + \beta_2 \text{ (lead)}_2 + \beta_3 \text{ (lead)}_3$$

$$z = \gamma_1 \text{ (lead)}_1 + \gamma \text{ (lead)} + \gamma_3 \text{ (lead)}_3$$

The coefficients α_1 γ_3 are known Multiplication of a lead by the e is achieved with an amplifier if the coefficient is greater than one and with a potentiometer if less than one Addition of terms is accomplished with a simple resistor network, and subtraction by means of a push pull amplifier An instrument can be designed to carry out these procedures and any desired coefficients may be used Hence, Becking Burger, and van Milaan[29] called the instrument a "universal vector cardiograph " An instrument of similar type has been constructed in this laboratory

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current lines it is possible to describe the properties of a given dipole completely by representing it by an arrow or vector whose direction is determined by the termini of these flow lines (fig 1B) The strength or moment of a dipole may be represented by drawing the vector with length proportional to the total number of current lines

Since each element of current flow passes through some portion of the conductive medium a potential field must be produced throughout the medium The magnitude of potential is directly related to the density of current lines at the point measured If points of equal potential are joined there is produced a new set of curves known as equipotential lines which intersect flow lines at right angles (fig 1A dashed lines) The potential at any point in this particular case is given by

$$V = \frac{M \cos \theta}{r} \tag{1}$$

where V is the voltage at the point M is the dipole moment r is the distance between the site of measurement and the dipole and θ is the angle between the dipole axis and the line r

The simplicity of using the dipole as an equivalent generator for the heart would be lost unless several further assumptions are made

1 The location of an equivalent dipole must be fixed throughout the cardiac cycle As a corollary the various surface potentials may be ex

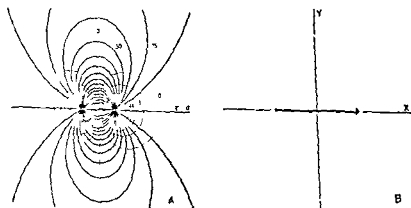


FIG 1 A depicts the current lines (solid) and equipotential lines (dashed) surrounding a source and sink of equal strength (small circles on the abscissa) in an infinite medium For clarity the separation between source and sink is made finite although in the case of a current dipole this distance is infinitesimal If the source which creates positive potential about it is the small circle on the left the dipole may be represented by a vector oriented as shown in B (A is from W R Smythe *Static and Dynamic Electricity* ed 2 New York McGraw Hill 1950 p 9)

7 Dipole Theory in the Analysis of the Electrocardiogram and the Vectorcardiogram

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A BASIC problem in electrocardiography is that of predicting the electrical activity within the heart from electrical measurements on the surface of the body. The chain of events within a single myocardial cell which culminates in an ordered sequence of release of electrical energy are understood fairly well (Chapter 1). It follows that each cell, during its electrical systole, is a miniature generator of current and, as such, may be expected to influence the voltage of the body surface. However, at each instant of electrical systole many myocardial cells in diverse sites are simultaneously active. The heart, at a given instant of time, may be described as cloaked in a pattern of voltages. Consequently, the potential at any location on the body surface is a summation effect in which the contributions of individual cells are well concealed. At best, surface potentials can be expected to provide only macroscopic correlations with cellular activity.

A logical approach to the analysis of body surface voltages is to determine whether their distribution over the body at each instant of time corresponds *to that which would be produced by a simpler generator than the heart*. Although an infinite variety of such generators can be imagined, the simplest is the dipole, a positive point charge (current source) separated from a negative point charge (current sink) by an infinitesimal distance (Chapter 5). It must be emphasized that the purpose of this substitution is merely to determine whether the body surface potentials are interrelated in some predictable manner. Although a given single dipole might be equivalent to the heart in the sense of producing a similar array of voltages over the body, an infinite number of more complex generators (the heart itself being one) would also qualify. There is also the possibility that two or more dipoles will be required to reproduce the distribution of body surface potentials. Discussion of this latter situation, which might be anticipated in the presence of circumscribed areas of myocardial disease, will be undertaken later.

Properties of a Current Dipole

A dipole may be regarded as a generator by virtue of the fact that it will cause electric currents to flow when placed in a conducting medium. These various current paths are plotted as solid lines in figure 1A. It will be noted that these paths or current lines must generally curve in order for all to originate at the source and end at the sink. Despite the curvature of the

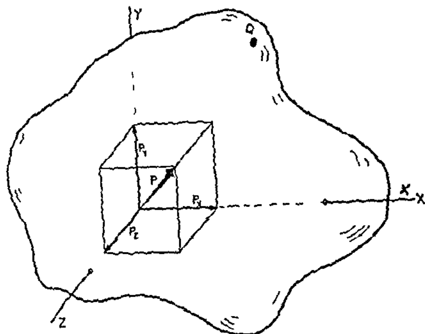


Fig 2 Spatially oriented dipole P arbitrarily locate l in a re i tive linear hetero g neou three dimen ional medium of irregula sh pe Orthog nal components P_x P_y and P_z are projected from P to the rectangular coordinates The equation fo the voltage V at point Q is $V_Q = C_Q P_x + C_Q P_y + C_Q P_z$ (Redrawn from Fr nk Ann New York Acad Sc 65 980 195)

variables as compared with the three of equation (3) In attempts to de vi e a boundary condition which more closely matches body contours other but no less complex formulae are available for ellip oidal media⁴ ⁶ It mu t be added that none of these equations can be applied to heteroge neous media

Application of element ry vector principles begun by Burger² and more fully extended by Frank¹ has provided a method of analy is (Chapter 5) which is free of the limitations noted above In figure 2 a dipole is repre ented by a vector (P) enclosed in a heterogeneous three-dimensional medium of irregular shape (such as the body) By projection on to the coordinate axes this vector may also be de cribed in terms of its x y and z components (P_x P_y and P_z) If the x component alone (P_x) were pres ent a voltage (V_Q) would be produced at any point (Q) on the urface (or within) The relation hip between V_Q and P_x may be expressed as follows

$$V_{Qx} = C_Q P_x \qquad (4)$$

plained by variation in the moment and direction of the dipole. A consequence of these vectorial properties of the dipole is that the changes in moment and direction occurring during one cardiac cycle may be graphically expressed in a compact form known as a vectorcardiogram (Chapter 6). *It is to be re-emphasized that in order to qualify as a truly equivalent* generator of the heart, voltages at all body sites must be predictable by appropriate analysis of these dipolar variations.

2. The *medium must be resistive, nonreactive and linear*, but it need not be homogeneous. Body tissues have been demonstrated to fulfill these requirements.[2]

3. Since electrocardiographic measurements are made on the surface of the body, which is surrounded by insulators (air, clothing, etc.) which prevent the loss of electrical energy to the environment, the medium is clearly finite. Relationships such as equation (1), which are valid for an *unbounded or infinite medium* must be modified so that *none of the current flow lines penetrate the boundary.*

It has been implied earlier that there are two general methods of investigating dipole induced potentials: (1) by potential formulae and (2) by vector analysis. The first of these has been widely used in electrocardiography but unfortunately can be applied only when there is no boundary or the boundary is a regular one. Analysis of the standard electrocardiographic *leads by the rules first proposed by Einthoven implies that the extremities* are equally spaced about a great circle of a spherical medium and that the heart is located at the center. In this bounded case a simple formula suffices

$$V = M \cos\theta \left(\frac{1}{r} + \frac{2r}{R^3}\right) \qquad (2)$$

where R is the radius of the sphere and the remaining symbols are *identical* with those of equation (1).

Furthermore, since we are usually concerned with potentials on the surface only, R equals r and

$$V = \frac{3M \cos\theta}{r} \qquad (3)$$

A major defect *in representations of this sort is that the heart is assumed* to be centrically located, a fact at obvious variance with the anatomic state of affairs. "Equivalent" dipoles derived from reference frames inscribed within spheres have correlated poorly with those derived from more accurate lead systems.[3] Equations which allow the dipole to be placed eccentrically within the spherical medium have been devised[4] to compensate for this lack of generality but are complicated by the need for thirteen

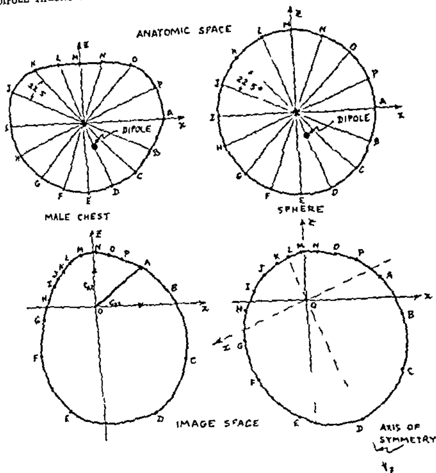


FIG 3 Similarity of image loops in the xz plane derived for a dipole equivalently located in (1) a male homogeneous torso model and (2) in a sphere The magnitude of the image coefficients (for example C_A and C_A) may be obtained for a lettered anatomic site by projecting the line from the origin to the like lettered image loop point on to the x or z axis (Modified from Frank [13])

surfaces obtained in models revealed fair agreement It is possible that the presence of the highly conducting blood mass within the heart in the former experiments accounts for the differences noted (Chapters 5 and 12)

Knowledge of the C values or image surface for a particular subject enabled Frank[13] to perform a unique experiment By examination of the image surface derived from a torso model of his subject, it was possible to devise leads whose potential is due to only one orthogonal dipole component

The following is an example of the procedure employed Utilizing the

where C_{Qx} is a proportionality constant whose magnitude is determined by the nature of the medium and the physical separation between the dipole location and Q *

Similar analysis applied in the case of V_{Qy} and V_{Qz} yields the relationships

$$V_{Qy} = C_{Qy}P_y \quad (5)$$

$$V_{Qz} = C_{Qz}P_z \quad (6)$$

When these three components act simultaneously, the voltage at Q due to the spatially oriented vector P will be the sum of the components acting alone or

$$V_Q = C_{Qx}P_x + C_{Qy}P_y + C_{Qz}P_z \quad (7)$$

The proportionality constants C_{Qx}, C_{Qy} and C_{Qz} for a given anatomic surface point can be obtained by use of equations (4), (5) and (6) separately For example, if the same unit of current were passed through a dipole located at the heart center and oriented successively along the x, y and z axes, the ratio of the voltage measured at the point Q to the current applied would give the value for C_{Qx}, C_{Qy} and C_{Qz} Experiments of this sort have been done in two ways Burger[7] and Frank[8] used models of human torsos filled with tap water and determined the C values for numerous anatomic points When plotted on Cartesian coordinates, the C values for multiple anatomic points form a curved surface, known as image space (fig 3 and Chapter 5) Each point in image space has therefore, a corresponding anatomic locus By projecting a heart vector on to the line drawn from the origin of this space to a given image point and multiplying the projection by the length of the line the voltage actually present at the corresponding anatomic site may be predicted It is significant that the shape of such a surface was not appreciably changed when inhomogeneities representing the lungs, etc were introduced into the model [7]†

In another set of experiments, C values were obtained in a living human subject by reciprocal stimulation of a dipole near the heart (within the esophagus)[9] and within the hearts of cadavers [10] Although the dipole location in these two latter experiments in or near heterogenous media (blood within the heart chambers) varied in the two experiments, the image surface in the two cases remained virtually unchanged Comparison with image

* *It may be helpful to note that since the dipole component* (P_x) *is derived from a current* dipole equation (4) is a form of Ohm's law C_{Qx} then is clearly related to the resistive relationship between the dipole current and the voltage (V_Q) measured

† *There is considerable evidence that the conductivities of thoracic tissue* (except fat and blood) are numerically close [2]

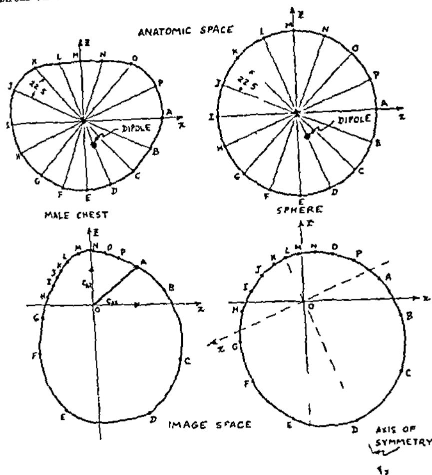


FIG 3 Similarity of image loops in the xz plane derived for a dipole equivalently located in (1) a male homogeneous torso model and (2) in a sphere The magnitude of the image coefficients (for example C_{Ax} and C_{Az}) may be obtained for a lettered anatomic site by projecting the line from the origin to the like lettered image loop point on to the x or z axis (Modified from Frank [33])

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The following is an example of the procedure employed Utilizing the

notation of equation (7), the voltage at two surface points, A and B, may be expressed as

$$V_A = C_{Ax}P_x + C_{Ay}P_y + C_{Az}P_z \quad (8)$$

$$V_B = C_{Bx}P_x + C_{By}P_y + C_{Bz}P_z \quad (9)$$

Since the C values are known for all surface points it is possible to choose point B on image space so that $C_{Ay} = C_{By}$ and $C_{Az} = C_{Bz}$. The line connecting A and B in image space will then be parallel to the x axis. The voltage of a lead measuring the difference in potential between these points would be

$$V_A - V_B = V_x = C_{Ax}P_x - C_{Bx}P_x + C_{Ay}P_y - C_{Ay}P_y + C_{Az}P_z - C_{Az}P_z$$

$$V_x = (C_{Ax} - C_{Bx})P_x \quad (10)$$

Since $V_A - V_B$ or V_x can be measured on the subject and C_{Ax} and C_{Bx} are known, P_x *can be calculated for each instant of time.* In a similar manner, P_y and P_z can be obtained. When the components so obtained were used to energize a dipole properly positioned within the model, the potential at any point (including precordial loci) could be measured on the surface of the model. The shape and amplitude of these synthesized leads matched to an astonishing degree those actually recorded on the subject from whom the model was derived. This experiment constitutes an example for the normal subject of the existence of a dipole equivalent for the heart. The dipole alone properly positioned at a fixed point in a homogeneous medium, completely sufficed to predict potentials observed at any point on the subject's body.

THE DERIVATION AND PROPERTIES OF ACCURATE ORTHOGONAL LEAD SYSTEMS

In the course of attempting to reproduce the surface potential of his subject by energizing the torso with a dipole, Frank[11] showed that dipole location was much more critical than the physical configuration of the torso. This relationship is illustrated in figure 3 where a dipole is positioned at a similar point in a transverse section of a torso model and in a transverse section of a sphere. Surprisingly, the image surfaces for the two shapes are very similar. Such observations suggested that it might be possible to derive orthogonal leads which would be suitable for use in subjects of almost any torso outline if sensitivity of the leads to dipole location were minimized. By carefully combining the potentials of seven body points whose image coefficients (C values) changed least as the dipole center was mathematically shifted throughout a cube 5 cm on each edge centered in the heart region of the model, such orthogonal leads have been devised[12]

(Chapter 6) Utilizing a physical dipole continuously moved over a similar volume in the heart region of a homogeneous torso Schmitt[13] has devised a similar lead system thought to be even more accurate This latter system combines weighted potentials from fourteen body sites (Chapter 6)

Inherent properties of such lead systems permit an analysis of situations in which body surface potential distribution may require the presence of more than one dipole within the heart region

The voltage of one orthogonal lead of such a system due to a dipole at one site within the heart region may be expressed as $V_{xA} = C_x P_{xA}$, where V_{xA} is the voltage measured by the lead P_{xA} is the x component of the dipole and C_x is the associated image coefficient If a second differently oriented dipole were simultaneously present within the cube about the heart region its voltage contribution to the lead would be $V_{xB} = C_x P_{xB}$ The C_x value is identical in the two equations because the lead system has been designed to be insensitive to dipole location The total voltage measured by this lead would be

$$V_{xA} + V_{xB} = V_x = C_x(P_{xA} + P_{xB}) \tag{11}$$

Similarly

$$V_y = C_y(P_{yA} + P_{yB}) \tag{12}$$

$$V_z = C_z(P_{zA} + P_{zB}) \tag{13}$$

where V_x, V_y and V_z are the orthogonal voltages due to both dipoles The correlation hips show that if two (or more) dipoles *were* present within the heart region orthogonal lead systems insensitive to dipole location would permit summation of the dipoles by vector addition

The foregoing principle has been stated in another manner by advocates of the lead field hypothesis[14, 15] In this latter theory currents are caused to flow across hydraulic models[15] or models cut out of conductive paper[15] Such models are of necessity restricted to two dimensions Voltage is applied to multiple surface points causing a current to flow through the model The surface points are chosen so that current flow in the heart region is in the form of straight parallel lines collinear with the x y or z axis (fig 4) Under these circumstances the Helmholtz reciprocity theorem reveal that the current lines surface leads and current generators in the heart area are interrelated (Chapter 5) The direction of any single current line indicates which component of a current dipole would be detected by the surface lead with which the line was originally created Since the current field (lead field) over the heart area of figure 4C consists of a group of straight lines parallel to each other and to the x axis the multiple surface leads with which they are associated will detect the x component of a

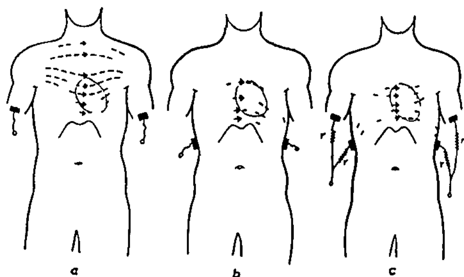


Fig 4 Current lines created in a flat model by voltages applied to the sites indicated In (a) and (b) the lines traversing the heart area are curved and nonparallel In (c) the lines are made straight and parallel by the use of multiple electrodes and weighting resistors (From McFee and Johnston Circulation [14])

dipole or dipoles located anywhere within the heart area of the model It is apparent that the voltage measured by this multiple electrode lead is a *function of the sum of the x components of all dipoles present within the* heart area of the model In effect this lead is equivalent to similar ones devised by application of the image surface technique previously described

General application of the 'lead field' is, however uniquely restricted in at least two ways (1) no three dimensional flow model has been devised (2) no analytic method of locating and weighting the required electrodes on irregular three dimensional surfaces is available

Precordial Leads and the Equivalent Dipole

The preceding remarks indicate that it is possible to devise orthogonal lead systems which extract a dipole even when there may possibly be multiple dipoles simultaneously present in the heart region Under these circumstances, the orthogonal leads of Frank and Schmitt act as though great distances intervene between these leads and the heart At distances large in comparison with the separation between the two dipoles (drawn as vectors in figure 5A) they would add vectorially and appear as their sum in figure 5B However if we are permitted to get close to the dipole pair of figure 5A, the similarity to the vector sum vanishes This fact may be clarified by comparing the two graphs in figure 6 One (A) is a plot of the potentials about these two dipoles oriented 90° apart and separated by a distance of 2A units The potential is calculated for points in the x y plane

lying at a distance 2A units from the midpoint of the line separating the two dipoles as indicated by the circle surrounding them in figure 5A. The potential function is asymmetrical and has four peaks. The potential distribution about the single dipole calculated for a circular locus of the same radius is a symmetrical sinusoidal curve (fig. 6B). Although these functions were determined with formulae for unbounded media, the dipole pair curve is quite similar to one obtained experimentally for a similar dipole pair in a bounded cylindrical medium.[17] It was shown earlier that the spherical surface potential distribution for the centric single dipole is similar in the bounded and unbounded cases (equations 1 and 3).

It might be logically deduced that precordial or esophageal leads which are physically close to the heart are apt to be at least partially influenced by local electrical activity which would be concealed in orthogonal distant leads. Under these circumstances a vectorcardiogram derived from accurate orthogonal leads would not be a complete representation of all electrocardiographic information. The single dipole extracted with such leads would not be an equivalent dipole. On the other hand, if, instead of multiple dipoles, a single dipole can be substituted for the heart, the use of leads other than the orthogonal set would provide no further clinical information. It is unfortunate that there is a paucity of data available to resolve this question.

In one normal case Frank[11] was able to synthesize standard and precordial leads from orthogonal components with about 85 per cent accuracy. It would appear justifiable to ascribe a considerable portion of the inac-

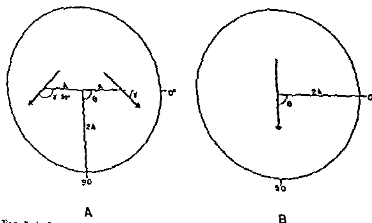


FIG 5 A Vectorial representation of two dipoles of equal moment B oriented 90 apart and separated by the distance 2A. The circle is the locus of points 2A units from the center of the line between the dipoles. B A single dipole of moment $\sqrt{2}B$ which is the vector sum of the two dipoles in A. The circle is the locus of points 2A units from the dipole.

curacy to unavoidable experimental error. This experiment leads to the conclusion that in Frank's subject all surface electrocardiograms could be accurately reproduced by a single equivalent dipole operating within the heart region. There exist two explanations for this unlikely dipolar behavior of a distributed generator as large as the heart. (1) It is reasonable to consider that *at any instant the depolarization front within the heart is semispherically shaped*. Analysis of the surface potentials created by (a) a semispherical array of dipoles immersed eccentrically within a spherical homogeneous conducting medium and (b) by a single dipole having the same eccentricity revealed little difference[18]. (2) Okada[17] has shown that if a highly conducting mass (heart's blood) is brought close to two simultaneously acting dipoles immersed within an otherwise homogeneous cylinder, the potential distribution about the cylinder changes from a multiple peaked curve to a shape similar to that due to a single dipole. In effect, the pres-

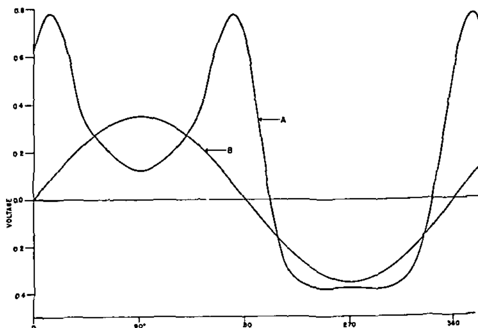


FIG. 6. Curve A is the voltage at all points on the circle surrounding the dipoles in figure 5A when they are immersed in an infinite homogeneous conductive medium. The voltage equation is

$$V = \frac{\sqrt{2}\,B}{2A^2}\left[\frac{2(\sin\gamma + \cos\gamma) - 1}{(5 - 4\cos\gamma)^{3/2}} + \frac{2(\sin\gamma - \cos\gamma) - 1}{(5 + 4\cos\gamma)^{3/2}}\right]$$

Curve B is a graph of voltages on the circle surrounding the dipole in fig. B. The voltage equation in this case is

$$V = \frac{\sqrt{2}\,B\cos\theta}{4A^2}$$

ence of the highly conductive mass transforms the asymmetric curve of figure 6 to the sinusoidal curve without recourse to "distant" leads.

It seems reasonable to assume that if the potential field about multiple dipoles is measured at a given instant of time, multiple sharp peaks may result if measurements are made from some points which are close to the dipoles. Figure 5A is a special case of this sort. It is implied that a similar excursion about a single dipole would reveal a single positive and a single negative peak. Unfortunately no rigorous proof of these assertions can be offered. Nelson[19] carefully measured the potential about the chest circumference at fixed intervals of time and showed that multiple peaks were readily obtained. Such an experiment appears to demonstrate the presence of multiple dipoles which could not have possibly been predicted from orthogonal "distant" leads. The magnitude of this multiple dipolar effect regrettably is not easily quantitated.

Cancellation Experiments and the Equivalent Dipole

As a consequence of dipole theory, there is an interesting relationship among the voltages at *any* four independent body sites. If a fixed locus *dipole*, varying only in moment and direction within a resistive medium, generates these voltages, each may be represented at a given moment by one of the following equations:

$$V_A = C_{Ax} P_x + C_{Ay} P_y + C_{Az} P_z \tag{14}$$

$$V_B = C_{Bx} P_x + C_{By} P_y + C_{Bz} P_z \tag{15}$$

$$V_C = C_{Cx} P_x + C_{Cy} P_y + C_{Cz} P_z \tag{16}$$

$$V_D = C_{Dx} P_x + C_{Dy} P_y + C_{Dz} P_z \tag{17}$$

It is possible to obtain an expression for P_x by simultaneously solving the first three equations (equations 14, 15 and 16). P_x then will be expressed in terms of V_A, V_B, V_C and the various C coefficients in these equations. P_y and P_z may be similarly expressed. If the values of P_x, P_y and P_z so obtained are substituted in equation (17), V_D will be related to V_A, V_B and V_C in terms of combinations of the C coefficients. In particular

$$V_D = \alpha V_A + \beta V_B + \gamma V_C \tag{18}$$

where α, β and γ are combinations of the C coefficients of equations (14), (15), (16) and (17). α, β and γ are consequently similarly dependent only upon body contour, dipole location and tissue heterogeneity. They are invariant with time.

The result of transposing V_D to the other side of equation (18):

$$\alpha V_A + \beta V_B + \gamma V_C - V_D = 0 \tag{19}$$

curacy to unavoidable experimental error This experiment leads to the conclusion that in Frank's subject all surface electrocardiograms could be accurately reproduced by a single equivalent dipole operating within the heart region There exist two explanations for this unlikely dipolar behavior of a distributed generator as large as the heart (1) it is reasonable to consider that at any instant the depolarization front within the heart is semispherically shaped Analysis of the surface potentials created by (a) a semispherical array of dipoles immersed eccentrically within a spherical homogeneous conducting medium and (b) by a single dipole having the same eccentricity revealed little difference[18], (2) Okada[17] has shown that if a highly conducting mass (heart's blood) is brought close to two simultaneously acting dipoles immersed within an otherwise homogeneous cylinder, the potential distribution about the cylinder changes from a multiple peaked curve to a shape similar to that due to a single dipole In effect, the pre

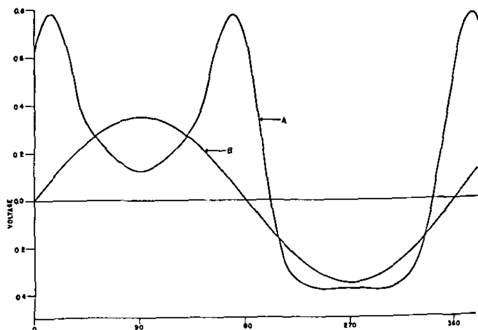


FIG 6 Curve A is the voltage at all points on the circle surrounding the dipoles in figure 5A when they are immersed in an infinite homogeneous conductive medium The voltage equation is

$$V = \frac{\sqrt{2}\,B}{2A^2}\left[\frac{2(\sin\gamma + \cos\gamma) - 1}{(5 - 4\cos\gamma)^{3/2}} + \frac{2(\sin\gamma - \cos\gamma) - 1}{(5 + 4\cos\gamma)^{3/2}}\right]$$

Curve B is a graph of voltages on the circle surrounding the dipole in fig B The voltage equation in this case is

$$V = \frac{\sqrt{2}\,B\cos\theta}{4A^2}$$

If we let

$$C_A = C_{R} + C_{YL}$$

and

$$C_B = C_{YR} - C_{L}$$

then

$$V_P = C_A P_{XR} + C_B P_{YR} \quad (28)$$

By similar analysis the voltage at several other points could be established in similar form (i e , in terms of P_{R} and P_{YR}) but with different C values for each case Such a set of equations may then be manipulated as were equations (14-17) and a successful lead synthesis or cancellation experiment would be predicted However it must be specified that the relationship of 90 between the vectors used here would have to be maintained with time Time variation of the moments of such dipoles would not spoil a cancellation procedure if the moments remained equal to each other at each instant

In general any number of interdependent dipoles whose moment and direction ratios are constant functions of time can be expected to exhibit the cancellation phenomenon Although physiologic considerations suggest that the occurrence of such dipole systems within the heart is unlikely cancellation experiments designed as a test for an equivalent dipole[22] must be interpreted with caution The only method yet devised as a theoretically perfect test for an equivalent dipole is the accurate replication of all surface induced potentials when the dipole is substituted for the heart At the moment such substitutions are best done with the aid of torso model

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indicates that these interlead relationships form the basis of cancellation experiments (Chapter 5) In such experiments four body voltages, including one from a precordial site, are suitably proportioned and combined to yield a null result[21]

Although the preceding relationships have been devised by manipulating the vectorial components of a single dipole, it cannot be inferred that the performance of a successful cancellation experiment or the synthesis of a given lead from three other independent leads (equation 18) proves the existence of a single equivalent dipole

In figure 5A, two dipoles are represented by vectors of equal moment directed 90° apart The voltage at a given point will record the contribution from both dipoles If the vector on the right furnishes V_R volts and that on the left V_L volts, it may be seen that

$$V_R = C_{xR}P_{xR} + C_{yR}P_{yR} \tag{20}$$

$$V_L = C_{xL}P_{xL} + C_{yL}P_{yL} \tag{21}$$

where C_{xR}, C_{yR} and P_{xR} P_{yR} are the image coefficients and dipole components of the right vector and similar terms with the subscript L refer to the left vector Let B equal the length or moment for each vector If γ is the angle between the right vector and the abscissa $\gamma + 90°$ is the corresponding angle of the left vector Then

$$P_{xR} = B \cos \gamma \tag{22}$$

$$P_{yR} = B \sin \gamma \tag{23}$$

and

$$P_{xL} = B \cos (90° + \gamma) = -B \sin \gamma = -P_{yR} \tag{24}$$

$$P_{yL} = B \sin (90° + \gamma) = B \cos \gamma = P_{xR} \tag{25}$$

therefore

$$V_L = C_{yL}P_{xR} - C_{xL}P_{yR} \tag{26}$$

But the voltage at the point (V_P) in question is the sum of contributions from both V_R (equation 20) and V_L (equation 26)

$$V_P = V_R + V_L = C_{xR}P_{xR} + C_{yR}P_{yR} - C_{xL}P_{yR} + C_{yL}P_{xR}$$

Therefore

$$V_P = (C_{xR} + C_{yL})P_{xR} + (C_{yR} - C_{xL})P_{yR} \tag{27}$$

8 Status of Leads Other than the "Standard" Leads

ADOLPH R. BERGER, M.D.

In Chapter 6 it was pointed out that errors are inherent in present methods of leading used in electrocardiography, and that the concepts of the lead vector and of the lead field give promise of the eventual refinement of leads which will satisfy not only the precise requirements of the biophysicist and of the engineer but also the pre ing and practical needs of the clinician. But it was also emphasized that certain practical considerations make it unlikely that an easily used, mathematically exact, and generally applicable clinical method will be forthcoming in the immediate future. Under the circumstances, it has seemed prudent to review the attributes and faults of the innumerable leads which have been designed empirically in the past for clinical use.

The pioneer electrocardiographers employed the term "lead" for a single pair of electrodes attached directly to the body from the recording apparatus. With the application of fundamental principles of potential theory to electrocardiography and with improvement in instrumentation, this definition of a lead may be modified to "a pair of terminals, each connected either directly or with any number of resistors to electrodes on the body."[1] Electrodes have been applied to innumerable loci on the surface or in the deeper regions of the body to derive the electromotive forces of the heart. Undoubtedly, Einthoven[2] early realized the need for some convention and uniformity in the new field and in 1906 he adopted the three bipolar extremity leads upon which so much of clinical electrocardiographic knowledge has subsequently been erected.

The most any system of electrocardiography can do is to indicate sequentially the orientation and magnitude of unopposed or uncancelled current dipole moments in the various areas of the heart from beat to beat. Theoretical speculation may indicate a particular system—scalar, vector or stereovector—for the optimum appreciation of such forces. However, the practical problem of clinical utility demands that the given system of electrocardiography yield consistently a highly accurate and valid record. Clinical usefulness likewise requires that the system be feasible technically.

The effect of condenser resistor networks, patient instrument circuits and response characteristics of the recording apparatus on the form of the electrocardiogram cannot be disregarded in an appraisal of the registration of special leads. On occasion an alteration (particularly in the final ventricular deflection) which seemingly is detected by the use of special leads may represent instrument or circuit induced artifact.[3]

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value The value of the esophageal lead may be enhanced by the simultaneous use of a standard lead The atrial intrinsic deflection, prominent because of the proximity of the exploring electrode to the atria can thus be distinguished from bizarre atrial or ventricular complexes in conventional leads

Among the interesting cases described by Kistin and Bruce[14] is one (Case 3) of atrial tachycardia (flutter) with varying atrioventricular block and alternating bidirectional P waves The need in some instances for the simultaneous registration of a conventional and an esophageal lead is evident Although small inverted P waves were visible in a conventional chest lead (V_1) during periods of increased atrioventricular block the alternating bidirectional nature of the P waves was seen only in the simultaneous esophageal lead Another example of the usefulness of esophageal leads in identifying atrial activity in a case of sinoatrial block with dissociation is shown in figure 1

Discussions of myocardial infarction are concerned almost exclusively with involvement of the ventricular myocardium The electrocardiographic features of such infarction are well known *Infarction of the atrial muscle* (which is found at autopsy in 7 2 to 17 per cent of subjects with myocardial infarction[15]) also should produce a sequential *pattern of change in* the atrial electrocardiographic *complex beyond that* resulting from disturbance of conduction or of rhythm Since it is unlikely that displacement of the atrial S T segment or inversion of T_p *could be seen well, if at all* in conventional leads juxta atrial esophageal leads should offer the best means to detect these aberrations However *records which demonstrate* such patterns in patients could not be found although examples were obtained from an electrocardiographic study of localized auricular necrosis induced in dogs by the intramural injection of 95% alcohol[16]

One of the six tracings is reproduced in *figure 2* Atrioventricular block was produced by the *application* of a clamp to the bundle of His The electrophysiologic *disturbances* which *resulted* from localized necrosis of the right atrium are well *depicted in* the esophageal lead The amplitude of the atrial intrinsic deflection *is reduced and* a Q_p wave is apparent There is convex upward *displacement* of *the atrial* S T segment T_p negative in the control tracing is positive

The esophageal lead was affected following necrosis of the wall of either atrium but the changes were more marked with involvement of the right chamber Although definite evolution *of* the atrial S T abnormality was observed in only one experiment individual elements of the total pattern were noted in almost all *of the* other experiments

Clinical application may be *made of* this fact In the patient with suspected anginal syndrome in whom *the* various cardiac stress tests *yield*

The conventional 12 lead limb and precordial scalar electrocardiogram, in large measure, has fulfilled clinical requirements in simple fashion, but sometimes, unfortunately, the information afforded by this type of exploration has been incomplete or inadequate. To overcome this deficiency, leads other than the 12 presently employed have been suggested. The points of application of the electrodes, it seems, have been limited only by the ingenuity of the electrocardiographer and by the surface area, internal or external, of the human body. Action currents of cardiac origin have been recorded from the alimentary tract, the bronchial passages, and from within the chambers of the heart itself. The currents have been obtained, too, from the surface and from within the wall of the heart exposed at surgical operation.

The supplementary leads presumably represent, in sum, the efforts of investigators to obtain more clearly the potentials of the atria and ventricles, to identify the sites of origin of cardiac rhythms, to elucidate the spread of the excitatory or recovery processes, and to detect myocardial "injury"* or hypertrophy unidentified by other means. Most often, it has been expedient to obtain such information by the use of esophageal, abdominal and additional thoracic leads.

Esophageal Leads

The alimentary canal was used early and extensively as a locus for the registration of myocardial action currents, particularly in animals (ano esophageal leads). Waller[4] in obtaining one of the first human electrocardiograms, placed an electrode in the subject's mouth and another electrode over the precordium or on an extremity; on another occasion,[5] he derived an oral rectal lead. He thus proved that the record (made with a capillary electrometer) represented a true electrical variation of the heart. The first human esophageal electrocardiogram was made by Cremer,[6] who inserted (under radiographic vision) an electrode into the esophagus of a sword swallower. However, esophageal leads were used infrequently, if at all, until 1934 when Lieberson and Liberson[7] reintroduced the method for clinical purposes; these workers used bipolar (esophageal left leg) leads. Subsequently, Luisada,[8] Brown,[9] Ramirez,[10] Taquini,[11] Nyboer,[1] Kistin, Brill and Robb[12] and others described the amplitude and configuration of the atrial and ventricular complexes at various esophageal levels, and employed the esophageal electrode as a semidirect derivation in clinical electrocardiography.

As an aid in the diagnosis of complex cardiac arrhythmias, particularly those in which electrical evidence of atrial activity is absent or unidentifiable in conventional leads, esophageal electrocardiography has great

* For definition see Chapter 12

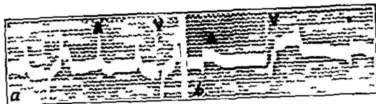


FIG 2 Effect of localized necrosis of the right atrium on the esophageal lead Mechanical atrioventricular block produced prior to the control tracing (a) After the intramural injection of alcohol (b) to be noted in the atrial complexes are the appearance of Q waves and elevation of the S T segment with upward bowing Standardization 10 mv = 1 cm (From Sander Am J Med Sc [16])

negative results an effort can be made to detect evidence of atrial ischemia To be sure it is unusual for coronary atherosclerosis to be so circumscribed that only the atrial muscle is affected by the reduced arterial flow yet, in selected instances such a disturbance possibly could be made evident by the use of esophageal leads

One additional use of esophageal leads is of interest If tracings are made from multiple points in the esophagus (or by the use of an intracardiac catheter from points in the right atrium) and recorded simultaneously with lead II so-called atriodiagrams may be constructed [17] The ratio of the P Q interval in lead II to the I Q interval (the interval from the beginning of the intrinsic deflection of the esophageal P wave to the onset of QRS in lead II) is calculated for each lead point The ratio eliminates variations due to rate The plot of the distance of each lead point from the diaphragm on the ordinate and the corresponding P Q/I Q ratio on the abscissa yields the atriodiagram The diagrams (fig 3) indicate that activation of the left atrium proceeds in a more or less transverse direction activation of the right atrium is in a craniocaudal direction (I Q interval shorter near base) Deformities in the diagrams are found with disturbances of intra atrial conduction and with atrial hypertrophy In the figure the diagram in mitral disease is fairly normal for the right atrium but bulges conspicuously to the left for the left atrium This is interpreted to mean that local impairment of conduction causes widening of the P wave in mitral disease

Earlier investigations to record simultaneously and separately electrical activity in the atria may be found in the review by Luisada [18] More recently Brown and Ellis[19] and Ellis et al [20] Kilpatrick[21] and Thomas and De Jong[22] have studied the atrial electrocardiogram in various types of cardiac disorders

The unipolar esophageal electrocardiogram obtained at the ventricular level has been employed for the diagnosis of ventricular myocardial disease The normal configuration of this derivation is well known to experienced

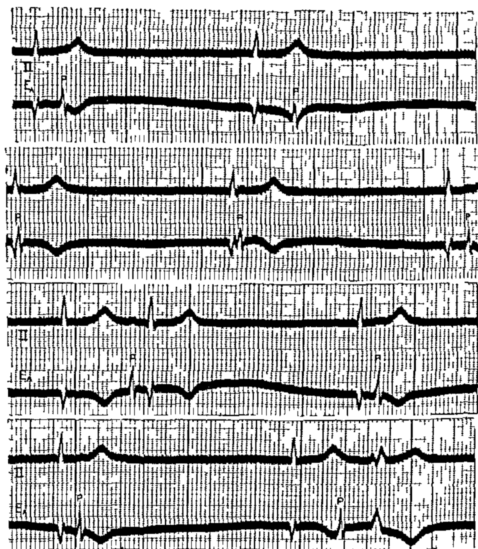


Fig 1 Simultaneously derived lead II (upper trace II) and esophageal lead at the atrial level (lower trace E_A) for both galvanometer sensitivity at normal (1 mv = 1 cm) These electrocardiograms obtained from a 66 year old white man illustrate a type of sinoatrial block Identification of the cardiac mechanism is possible with certainty only with the use of the esophageal lead The upper two strips are continuous Sinus arrhythmia and bradycardia and idioventricular rhythm are present the sinoatrial center always discharges at different separating intervals from the idioventricular center In strip three a sinoatrial excitatory process is transmitted normally to the ventricles producing interference In the final strip the bizarre ventricular complex is identified as an aberrant QRS complex in response to supraventricular excitation the P wave seen clearly in E_A cannot be distinguished in the standard lead (From Kossmann J Chronic Dis 4 434 1956)

inaccurate positioning of the exploring electrode—come to mind Certainly extreme care must be exercised in the placement of the electrode Fluoroscopic check of its position (which should be at least 7 5 cm below the level of the last intrinsic P wave) will avoid the error of malplacement

Evaluation of the ventricular esophageal electrocardiogram was made by Rubin et al[46] Sixty four patients with clinical and electrocardiographic evidence of posterior myocardial infarction were studied The esophageal lead did not demonstrate the lesion in 12 per cent in 7 per cent it was the only lead to exhibit abnormal Q waves which were not seen in lead aV_F Despite the occurrence of false positive Q waves in lead aV_F Rubin et al stated that this lead was more consistent than the esophageal derivation in the demonstration of the presence of posterior myocardial infarction Oram et al[49] likewise concluded from their clinical investigation of 126 cases of posterior myocardial infarction that lead V_F is slightly superior to the esophageal lead for the diagnosis In Burchell s experience[44] when a deep Q in lead III was the only finding which raised the suspicion of old myocardial infarction the esophageal leads frequently yielded equivocal findings

Leads from the Thorax and Abdomen

Since the description of Waller s original chest lead many thoracic leads have been employed for the detection of ventricular myocardial disease Indeed the greatest number of supplementary leads have been introduced for that purpose and a comprehensive consideration of the subject may be found in the monograph by Crewin

Two main groups of additional leads are recognized One group consists of a heterogeneous assortment of chest derivations of most diverse natures usually bipolar with varying exploring and indifferent electrodes taken at scattered planes and levels of the thoracic cage Most of these leads were introduced prior to 1938 at which time a special committee (created by the American Heart Association and the Cardiac Society of Great Britain and Ireland to end or at least lessen the then existent confusion) recommended the nomenclature and usage currently employed In the other large group the unipolar conventional precordial leads[3] are supplemented by exploration of the chest at the same cross sectional level or at higher or lower levels or by exploration of the right hemithorax or the back or by exploration of the supraclavicular fossae and the abdominal wall

In this brief survey it is impossible to present even in summary fashion all the leads of the first group or even to do justice to selected examples The results of Groedel s extensive thoracic explorations and his concept of

electrocardiographers, as is the fact of a certain variability of ventricular potentials at the diaphragmatic level.[60] Although criteria have been outlined for the normal and infarction "patterns" of esophageal electrocardiograms,[12] the precise interpretation of deep Q or inverted T waves in esophageal tracings obtained from presumably normal subjects and recorded at the "ventricular" level often is a difficult problem. Several possible explanations—marked elevation of the diaphragm and resultant rotation of the heart, variation in the usual cardioesophageal anatomic relationship, and

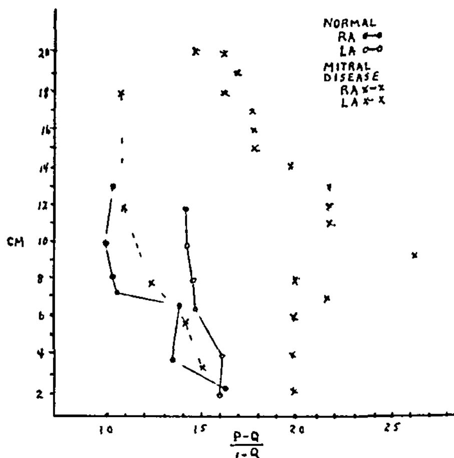


Fig 3 Atriodiagrams of the right and left atria constructed from the values obtained from a normal subject and from a patient with mitral valve disease. Ordinates: heights (in cm) of the points of recording above the diaphragm. Abscissae: the IQ/iQ ratios. A slope from the left upper to the right lower corner of the figure indicates activation of the respective atrium in a craniocaudal direction. Note that this pattern exists for the normal right and left atrium and for the right atrium of the patient. However, in the latter case the esophageal left atriodiagram extends markedly towards the right at levels 6–14 cm above the diaphragm, a finding consistent with local delays in conduction in the affected chamber. (Adapted from Wenger and Hoffmann Credner.[17])

to conventional leads I II and III and presumably reflect the potentials of the posterior anterior and diaphragmatic surfaces of the heart respectively. According to Nehb the general configuration of his leads resembles the standard leads and inversion of a wave signifies an abnormality. However Frost[?] found several instances of low or isoelectric T_J waves, and Pollock[?] noted inversion of this wave in 4 per cent of 50 normal subjects. Grewin described several rather low T_D waves in dubiously normal subjects. More important however was his demonstration of the importance of accurate placement of the electrodes: significant variations (appearance of deep Q or inverted T waves) were induced by slight shifts in electrode positions.

The alterations in the Nehb leads which accompany ventricular hypertrophy or myocardial infarction are similar qualitatively to the changes which occur in the conventional leads. It is most improbable however that the special leads exhibit abnormalities not present to some degree in the usual twelve leads. In only one of 85 cases examined by Frost[?] were Nehb leads abnormal in the presence of normal standard and precordial leads. Pollock[?] found in 30 patients with recent myocardial infarction no changes evident in the special leads which were missed in the conventional 12 lead exploration. In a limited experience (10 cases) the same results were obtained.[30] Although Lepeschkin stated that the small heart triangle revealed myocardial abnormality not evident in the standard leads or in lead CF_4 in 37 per cent of cases data from Grewin indicate that the use of additional chest leads or extremity potentials would reduce this figure to 5 per cent or even to 1.5 per cent. Very infrequently, as seen in the illustration published by Holzmann and as suggested by others[29, 31] the changes due to myocardial infarction may be demonstrated more clearly by the Nehb leads than by the conventional leads. The assertion by Slapak and Partilla[?] that their modification of the Nehb leads would make evident either earlier or uniquely 5 to 10 per cent of posterior wall infarcts was contradicted by Papp and Smith.[33] The latter workers showed persuasively that Slapak Partilla leads really represented physiologic left intraventricular leads obtained through the mitral orifice. In short the Nehb leads have been used infrequently (to judge by the published reports) and they offer no significant advantage over the 12 lead exploration program.

The same comments apply to the leads suggested by Condorelli.[34] These leads are AP (anteroposteriore) from the center of the sternum to a point on the back level with that center; E D (derivazione equatoriale destra) between the left subclavian fossa and the right posterior axillary line at the level of the seventh rib; and F S (derivazione equatoriale sinistra) between the right subclavian fossa and the left posterior axillary line at the level of

the dextrogram and sinistrogram, fill two volumes.* Other investigators have described as many as 28 and 44 chest leads. Details which are lacking in these abbreviated comments may be found in the original publications or in Grewin's monograph.

Ackermann,[24] using needle electrodes, derived three bipolar leads: A, from the second right intercostal space next to the sternum to the cardiac apex, B, from the same intercostal site to the fifth right intercostal space at the sternal border, and C, from the second right intercostal location to the projection of the apex on the back. These leads simulate the standard limb leads; lead B exhibits a P wave which resembles one of intra-atrial origin. Very little clinical information was given by the author and apparently no further use was made of his leads.

By placing the right arm and left arm electrodes in the corresponding axillae, Whitten[5] in 1937 obtained "intensified" leads in which the normal waves were similar to those of the corresponding bipolar extremity lead. In a small group of patients the special lead was altered by myocardial infarction in a fashion similar to the conventional lead; however, the changes were stated to appear "more readily" and "earlier." At the present time, these leads are no longer in use.

In 1938 Nylin and Sallstrom[6] described three synchronized leads between fixed points on the projection of the heart on the chest wall. The loci on the anterior wall were (1) the angle between the right atrium and the right vascular arch, (2) the angle between the pulmonic arch and the left auricle, (3) the cardiac apex, (4) the cardio-hepatic angle. On the posterior wall the lead points were (1) the angle between the right vascular arch and the atrial arch, and (2) the apical projection. The special leads (which practically coincide with the anatomic axes of the heart) in a small series of cases with myocardial infarction revealed changes, as might be expected, in several patients whose standard leads were uninformative.

The "small heart triangle" proposed by Nehb[7] in 1938 was created by a bipolar pattern of chest leads and apparently was intended to explore surfaces of the heart as large as feasible. Save for the points of contact the connections for the small triangle are similar to those for the conventional limb leads. The right arm lead is attached to an electrode at the junction of the second right rib with the sternum; the left arm lead electrode is located at the projection of the cardiac apex on the posterior axillary line (or at the scapular angle); the left leg lead is connected to an electrode at the apex. The three Nehb leads, D (dorsal), A (anterior) and J (inferior) correspond

* Kienle's interesting and comprehensive elaboration of "Funktions-Elektrokardiographie" includes leads from some hundred precordial coordinates and their complicated mathematical analysis.

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the seventh rib Review of the results obtained through the use of these leads by Ambrosio[35] and others is the basis for the comment made above Although these leads do not appear to be used any more for routine clinical electrocardiography, they have been employed on occasion to derive vector cardiograms by calculation

Cossio and Bibiloni[36] have described three bipolar leads which form an equilateral triangle in the horizontal plane at the level of the electrical center of the heart The electrode positions are the sternum at the level of the fourth intercostal space and the horizontal projection of this plane upon the left and right posterior axillary lines The resultant leads, designated H_1, H and H_3, afford a vectorial interpretation of the electrocardiogram in the selected plane The patterns of the normal and abnormal tracings obtained by this method parallel those observed in the conventional leads Until further experience with this method is available, accurate appraisal of the method's utility must be deferred However, if the information yielded by these leads is similar to that given by the Arrighi[37] leads,* clinical electrocardiographic diagnosis probably will not be advanced sig nificantly This suspicion stems from the observations of Brumlik and Kossmann[35] on frontal and sagittal electrocardiograms in subjects during an experimentally produced phase of lowered blood pressure

In the technique termed 'simplified (ABC) electrocardiography" Trethewie[39] has employed only three leads taken with a common origin (X) *at the xiphisternum X (corresponding to the left arm wire in standard lead* I) is paired with M (manubrium sterni), R (right chest at the base) and I (left axilla), MX LX and RX are leads A B and C respectively Trethewie claimed that his leads were always abnormal when the conventional leads were abnormal and that they might reveal changes consistent with the clinical picture when the Einthoven and Wilson leads are negative or equivocal " The illustrations in the article are not clear and the evidence to support the claims is not immediately apparent In the absence of per sonal experience with the method no comment can be made though one can imagine that these leads, like Nehb or similar leads on rare occasion may exhibit a certain increased sensitivity to the presence of myocardial abnormality

The conventional unipolar precordial leads have been augmented by ex tended exploration of the chest in certain patients In almost all instances the special *leads were introduced to lessen the small but apparent discrep* ancy between the anatomic changes denoted (or undetected) by the con

* Arrighi leads and the sagittal triangle are derived from electrodes placed in the left submaxillary region on the back opposite the center of the cardiac projection as seen by x ray and on the abdomen 3 or 4 cm to the left of the midpoint of the line joining the symphysis pubis and the umbilicus

ventional leads and the clinical histories or cardiac lesions demonstrated at postmortem examination Electrocardiographic evidence of hypertrophy or of delayed activation of the right ventricle may be adduced by additional right precordial leads Changes diagnostic of myocardial infarction may be evident in extra left precordial leads and the extent of the infarct may be defined more clearly

The necessity for such leads was recognized by Wilson and his associates[40, 41] They demonstrated 'diagnostic' patterns in tracings obtained at the intersections of horizontal lines at the level of the sternal end of the second third and fourth intercostal spaces with vertical projections through the usual left precordial points Subsequently, Myers[4] who designates these as HV leads also took high leads over the right precordium He made use too of leads V_7 and V_8 at the conventional and lower levels of the back Other investigators have employed supraclavicular[43] esophageal[44, 45, 46] and abdominal leads[47]

Myocardial infarction always produces the same fundamental changes in the ventricular complex However the leads in which these changes are best appreciated are determined not only by the size and location of the infarct within the heart but also by the precise orientation of the heart with respect to the external lead points In their respective studies of the transmission of cardiac potentials Wilson et al[48] described the relationship of limb to multiple precordial leads and the Wolferth group[49] usually could demonstrate the pathways of spread from a point near the heart into an extremity or to below the diaphragm along which the ventricular complex remained fairly uniform in appearance Implicit in these observations is the fact that the conventional leads will indicate the need for and the type of further electrocardiographic exploration

The form of the special lead is determined by the potential variations across the wall of the subjacent chamber Consequently the form is affected by displacement or rotation of the heart as well as by intrinsic myocardial disturbances Leads V_{3R} to V_{6R} often are needed for the reliable appraisal of counterclockwise rotation about the long axis which displaces the anterior transitional zone to the right Predominant left ventricular patterns in posterior axillary and back leads with right ventricular configuration of V_4 or V_5 denote clockwise cardiac rotation Under normal conditions V_7 and V_8 and HV_6 HV_7 and HV_8 (lead which oppose the left aspect of the base of the interventricular septum) exhibit small q waves by virtue of the left to right septal activation HV_1 and HV_2 reflect right ventricular activity HV_3 HV_4 and often HV_5 are in the transitional zone The T waves of the special left ventricular leads are similar in appearance to those of the conventional precordial leads Occasionally the T wave may be low or flat in axillary or back leads if the initial ventricular deflection is of low

amplitude, and inverted T waves are encountered normally in leads derived from the region of the atrioventricular sulcus (HV_8, HV_9 and V_9) *

Unipolar leads recorded at the tip of the ensiform cartilage (V_E) normally show rS, RS, Rs or R forms in the ventricular complex, with isoelectric or slightly elevated S T segments and well defined, positive T waves (rarely low or negative T waves), Q or QS waves are not seen [3, 4] The form of the tracing obtained midway between the ensiform and the umbilicus (V_{E0}) basically is similar to that of V_F though the T wave is more likely to be low or flat The tracing derived at the umbilical level (V_0) usually resembles leads aV_F or III It is possible for a Q or QS deflection to appear as a normal variant in V_{F0} or V_0 if the heart is in the horizontal electrical position

An augmented program of electrocardiographic exploration undoubtedly is of clinical value under certain circumstances Unfortunately, there is no large scale or statistical study of all of the additional leads (comparable to Grewin s investigation of some supplementary leads) to define those circumstances completely Apart from theoretical considerations therefore, evaluation of the extra leads becomes a matter of culling examples of their usefulness from the pertinent literature

Rosenbaum et al [40] reported (without autopsy confirmation) six cases in which the conventional leads did not furnish unequivocal evidence of myocardial infarction evidence which was afforded, on the other hand, by high thoracic exploration No indication was given of the frequency with which such additional study might be required However the value of this type of investigation was supported by Hecht[51] who summarized the results of a study of 86 cases of infarction of the lateral wall

Myers and co workers[5] correlated the electrocardiographic findings and the anatomic lesions found at autopsy in 161 cases Lateral wall ' infarction was noted in 105 hearts and was confined to this region in 27 Special leads were available in four cases In one case the high precordial leads were pathognomonic of the high lateral infarction found at autopsy the other leads were equivocal or suggestive In three cases special leads (in conjunction with the usual leads) were helpful in making the diagnosis and in outlining the position of the infarct

However Dunn Edwards and Pruitt [53] who reviewed the electrocardiographic findings in 30 cases of infarction of the lateral wall of the left ventricle, concluded that additional high left precordial and axillary leads were not especially helpful These leads merely repeated changes already evident in conventional leads (especially aV_L) they were normal if the usual leads were normal The experience in this laboratory has been similar to that of Dunn et al

* An example of the use of special high anterior chest lead is seen in figure 4



Fig 4 Lead taken at the horizontal level of the third intercostal space at sternal edge (3V1 to 3V6) which show to better advantage the elevation of the S-T segment seen only in lead V2 of the conventional chest lead. The patient, a 5[illegible] year old white male, had recently been in an auto accident and suffered injury to chest. However, a control electrocardiogram four years earlier showed an identical form of QRS and T in the same leads. A possible cause was a local chronic lesion near the base of the left ventricle or anterior septum, such as a calcified tubercle. There was much calcium in the hilar and paratracheal nodes. However, such records have been observed without other evidence of heart disease.

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PART III SPREAD OF EXCITATION AND OF RECOVERY, NORMAL AND ABNORMAL

9 Endocardial, Myocardial and Epicardial Leads in Man, Current Concepts of the Spread of Excitation and Recovery in the Ventricular Wall

CHARLES E KOSSMANN, M D

UNTIL RECENTLY there was more or less general acceptance and satisfaction with Lewis concepts[1] regarding the spread of excitation both in the atria and in the ventricles Based on data collected by him and his associates in dogs[2,3] the rate of spread of excitation in the atrial muscle was estimated to be 1000 mm/sec in the Purkinje system 4000 mm/sec, and in the ventricular walls 400 mm/sec Spread through the last was said to occur at the slow rate from endocardium to epicardium in a radial fashion Further it was intimated that the interventricular septum was excited almost equally from both sides with the left side slightly earlier than the right (figs 1 and 2)

As a result of recent experiments in several laboratories however the details of this concept have been challenged The principal points of difference concern the ventricles and may be stated as follows (1) the midportion of the left side of the interventricular septum rather than the base is excited initially and a considerable portion of it excited from below upward (refs 4 5 and Chapter 10) (2) a variable proportion of the subendocardial myocardium is excited at the same time and the remainder more slowly rather than in a uniform endo-epicardial manner (3) there is a physiologic barrier between portions of the septum excited from either side which becomes manifest when unilateral block is produced (ref 6 and Chapter 10) Since there is at present no universal agreement on the validity of these challenges especially the second and since the details of the experimental data from different sources varies a review of the present status of the spread of ventricular excitation is in order In this review it must be kept in mind that some of the observations have been made on the human heart but more have been made on the dog s heart with human inferences extrapolated from the latter

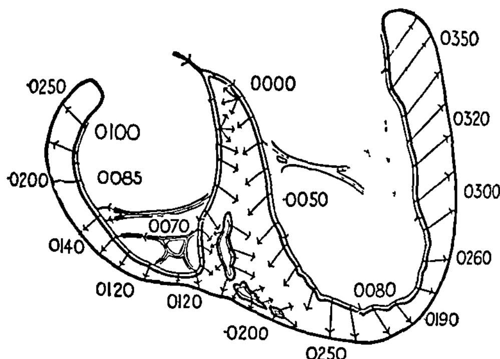


FIG 1 Lewis' diagram of the dog's ventricles as seen in section illustrating the direction taken by the wave of excitation The number opposite endocardial and epicardial points indicate the approximate times in seconds at which the wave arrives at each after the beginning of the electrical disturbance To be noted is that some of the arrows indicating the direction of the wave of excitation are directed upward in the base of the interventricular septum (From Lewis Phil Trans Roy Soc [1])

ENDOCARDIAL LEADS

By endocardial leads are meant those made from the interior of the heart with the electrode either against the endocardium (endoelectrogram) or separated from it by the heart's blood Many studies of this type have been made in animals in the past but with the introduction of the cardiac catheter it has been possible to explore the cavities of the upper and lower chambers of both sides of the heart of man [7,17]

The essential features of the records from the normal heart have been presented in several publications A summary of a frequent finding is shown in figures 3 and 4 [16]

Atrial endocardial potentials The atrial accession process is characterized by one or more intrinsic deflections depending upon the site of the exploring endocardial electrode Since excitation in the atria spreads in a radial fashion from the sinoatrial node atrial muscle may be regarded as a "plane" lamina rolled into a roughly bispherical shape It is reasonable

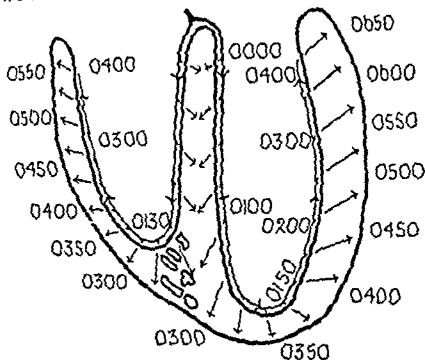


Fig. ᵃ Lewis diagram of the human heart with directions and time of endocardial and epicardial excitation which he deduced with some pretence to accuracy from his observation on the dog's heart. In contrast to figure 1 no basally directed vectors are indicated in the interventricular septum (From Lewis T The Mechanism and Graphic Registration of the Heart B at ed 3 London Shaw and Sons 1924 fig ( )

to expect therefore that records from the endocardial surface (modified perhaps by the heart's blood) will simulate those obtained from the epicardial surface or near it (*cavity leads*) This is actually the case and in leads from branches of the right pulmonary artery and the pulmonary *term* (fig 3 V_{RPA2}) as in esophageal leads and occasionally in right sided chest leads intrinsic deflections can be identified In an appropriate *record* the biphasic (or bipolar) *processes of* both accession and regression can be seen Of interest too is that *an after* potential or U wave has been found in atrial electrograms (ref 16 and Chapter 11)

The ventricular deflections *recorded from* the right atrium have been of considerable interest from the *standpoint* of their origin So far as the *upper* part of the right atrium is *concerned* the ventricular deflections *encountered* are in general similar to *those in the* lead from the right arm On *the other* hand large positive deflections may occur in the lower part which often

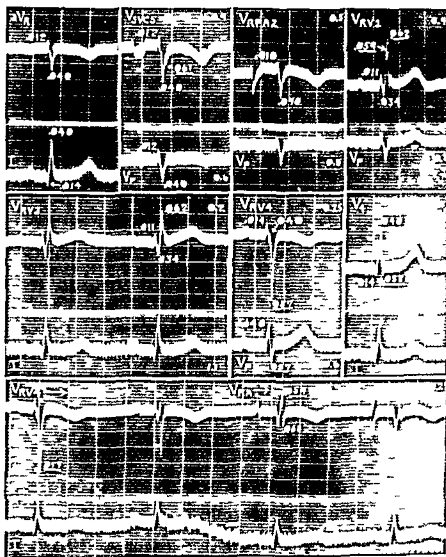


FIG 3 Patient My, female 69 A variety of internal and external leads recorded simultaneously with lead I (I) or with a lead (V_P) taken with a precordial electrode directly over the intracardiovascular electrode are shown The records in the first two rows have been arranged approximately in the order of their occurrence as a line is followed on or in the thorax from the right arm to the left side of the precordium Each lead is indicated by the symbol V followed by a subscript of letters and a number The letters indicate the structure from which the lead was made The number corresponds to the number of the intracardiac point as seen in figure 4 For example V_{SVC5} means potential of the superior vena cava at point 5 V_{RPA2} potential of the right pulmonary artery at point 2 V_{RV1} potential of the right ventricle at point 1 V_{RA} potential of the right atrium at an unknown location The number written at the right end of each trace denotes the sensitivity of the string at which it was recorded If left blank it means that the sensitivity of the string was normal (1 mv = 1 cm) Time lines occur every 0 2 sec

The remaining numbers on the record indicate the time of the adjacent QRS

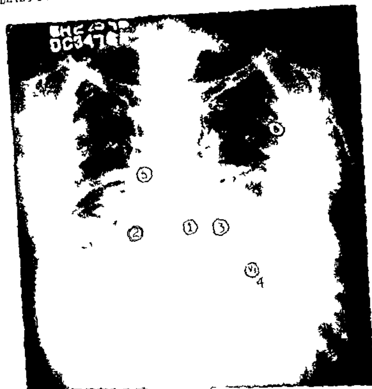


Fig 4 Teleroentgenogram of patient APv (figure 3) a 60 year old woman convalescing from bronchopneumonia but with no evidence of heart disease The single circles with a figure within indicate the approximate location of the intracardiac electrode at the time the electrocardiographic record was made The double circle around the number 2 indicates that the electrode was in a branch of the right pulmonary artery Point 4 (in the apex of the right ventricle) was directly under (in a P A view) the precordial lead V_1

Fig 3 —*Continued*

deflection with respect to the *beginning* of QRS in lead I Those waves which are simultaneous with the large positive deflection encountered in leads V_{RV1} and V_{RV2} at the base of the right ventricle are p [illegible] The wave und r consid ration in lead V_{RVC} is a negative *notch* on the ascending limb of S and *cannot* be identified at all in lead aV_R The intraventricular lead differ from the usual in the occurrence of a positive P wave in leads V_{RV1} and V_{RV2}

The lowest row shows continuous record made simultaneously with lead I as the electrode was withdrawn rather rapidly from the apex of the right ventricle through the tricuspid orifice into the right atrium The *time* of the S wave at the apex of the right ventricle (*first* complex) is almost identical with the *time of the* positive deflection seen as soon as the electrode has entered the right atrium (third complex) Location of the electrode in the latter chamber at the time is deduced from the initial occurrence of a diphasic P wave in the record (From Kossmann *et al* Circulation [18])

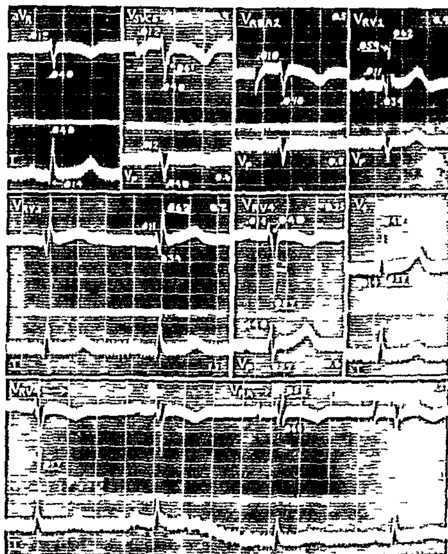


FIG 3 Patient A.P.V. female 69 A variety of internal and external leads recorded simultaneously with lead I (I) or with a lead (V_P) taken with a precordial electrode directly over the intracardiovascular electrode are shown The records in the first two rows have been arranged approximately in the order of their occurrence as a line is followed on or in the thorax from the right arm to the left side of the precordium Each lead is indicated by the symbol V followed by a subscript of letters and a number The letters indicate the structure from which the lead was made The number corresponds to the number of the intracardiac point as seen in figure 4 For example V_{SVC5} means potential of the superior vena cava at point 5 V_{RPA2} potential of the right pulmonary artery at point 2 V_{RV1} potential of the right ventricle at point 1 V_{RA} potential of the right atrium at an unknown location The number written at the right end of each trace denotes the sensitivity of the string at which it was recorded If left blank it means that the sensitivity of the string was normal (1 mv = 1 cm) Time lines occur every 0 2 sec

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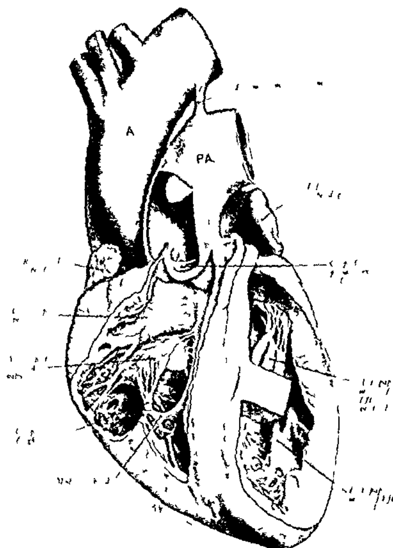


Fig. a. A drawing of the interior of the ventricles of the human heart, seen from the front, to show particularly the location and relations of the crista supraventricularis. (From Wamsley, T., Quain's *Elements of Anatomy*, ed. 11, London, Longman, Green & Co., 1929, vol. IV, part III, fig. 30.)

have no exact counterpart in relative magnitude in surface leads. In the normal an initial positive deflection in QRS is usually simultaneous with other deflections ascribed to early depolarization of the left side of the interventricular septum. A large negative deflection in any part of the atrium is usually simultaneous with the peak of the R wave in leads obtained from *the left side of the precordium and with the S wave or a notch on its descending* limb in the right ventricular endoelectrogram. It is produced, therefore, by excitation of the free wall of the left ventricle. Late, positive ventricular deflections of large or moderate size, usually in the lower part of the atrium, are ascribable to some considerable mass of muscle excited from below upward and from left to right, such as the crista supraventricularis in the roof of the right ventricle (ref. 16 and fig. 5) or the basal portion of the interventricular septum. It was thought originally that hypertrophy of the former structure might account for large, late positive deflections in right sided precordial leads *when there is increased work of the right ventricle* or right bundle branch block. A careful study by Emslie Smith[17] fails to confirm this belief, and it seems to indicate, from the two illustrations shown, that the late R wave in lead V_1, in mitral stenosis and pulmonary stenosis at least, occurs before the late intracardiac R wave. Actually, the latter is simultaneous with the S wave in lead V_1 in the examples given. In the normal subjects studied[16] this was also true, the nadir of the S wave in *the cavity lead from the right ventricle and in both the right and left sided precordial leads being simultaneous with the peak of the late intracardiac* R wave. The relation of the latter to surface deflections in right bundle branch block is not certain. Reasoning from what is known thus far, it would seem to account for the broad S wave seen with this conduction defect in leads reflecting the surface of the left ventricle and probably for a part, at least, of the R′ deflection in right precordial leads (Chapter 10).

There are two digressions which can best be made at this point. The first concerns again the general problem of local versus dipolar effects of the heart (Chapter 7). The atrial deflections obtained by leads close to the atrial muscle are different than the P wave in a bipolar lead made from the surface. Further, although an electrode close to the muscle will yield extrinsic effects, the intrinsic deflection will vary in time depending on the location of the electrode. The latter, at least, must then be regarded as a strictly *local effect (Chapter 6). The second digression revolves about the* exact part of the intrinsic deflection which marks the *arrival* of excitation under the exploring electrode. There are some direct measurements in this regard[18, 19, 20] but, analytically,[21] depolarization begins just *after* the beginning of the intrinsic deflection and is completed at the end. By means of a simultaneous differential lead, it has been shown by Durrer[18] that the differential spike occurs at the beginning of the fast portion of the intrinsic

Sano and associates [9] with simultaneous intracellular and nearby epicardial leads find a variable location on the intrinsic deflection of the latter signalling arrival of excitation (tortoise ventricle) Since the entire process of depolarization consumes perhaps 3 milliseconds in the human atrium [16] the errors involved by taking any particular part of the intrinsic deflection as an index of the beginning of depolarization are probably small

Ventricular endocardial potentials It is usually said that a record from the inside of the right ventricle will yield an initial summit resulting from early excitation of the interventricular septum from left to right a deep negative deflection due to excitation of the free wall of the left ventricle and an inverted T wave This can perhaps be regarded as an average potential of the cavity but a meticulous study made by the technique of recording while the catheter-electrode is moving[18] from one intracardiac site to another will reveal numerous variations in form of QRS within the ventricle (fig 3) Further a careful measurement of the nadir of the S wave will reveal that it is not often simultaneous with the peak of the R wave in left precordial leads but that a notch on its descending limb is Lastly positive deflections of considerable size may be encountered in leads from the base of the chamber [16, 17] As noted above these probably result from late excitation either of the crista supraventricularis or of the base of the interventricular septum

Records from within the normal left ventricle are more consistent in form and consist of a deep depression and inverted T wave [2] although at least one record made with a needle electrode pushed through the wall of the human heart showed an upright T wave [3] Timing of the nadir of the QS has not been carefully made In left bundle branch block the QRS will reveal an initial positivity or slurring of the downstroke of QRS (ref 22 and Chapter 10)

It is likely that there are variations in the sequence of excitation of the normal ventricles which account for some of the interindividual variations in the normal electrocardiogram (Chapter 10) An approximate schema of one type of normal is shown in figure 7

Myocardial Leads

Because the older data on the spread of excitation through the walls of the ventricles are based on measurements made at the endocardial and epicardial boundaries groups of investigators working in the laboratories of Prinzmetal [23-5] Scher [6-9] Durrer [18] and Sodi Pallares [30] have undertaken to study the electric potentials within the muscle (intramural potentials) All of these studies have been made with some variation of a stab or plunge electrode Both unipolar and differential records have been made the experimental animal has usually been the dog but some observations have

deflection and that there are initial and final slow portions (fig 6) Sodi Pallares and his associates[19] take the end or near end of the deflection for timing purposes The end of the intrinsic deflection marks the completion under, rather than the arrival of excitation at, the exploring electrode

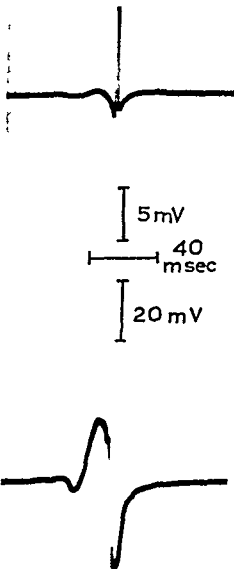


FIG 6 A spatial differential epicardial lead (above) recorded simultaneously with a unipolar epicardial lead made between one of the differential electrodes and the left leg of a dog The distance between the differential electrodes was 0 1 mm The spike of the differential lead is simultaneous with the fast portion of the unipolar lead The initial and final slow portions of the intrinsic deflection in the latter are to be noted *(From Durrer and van der Tweel Am Heart J* [18])

been made in man.[3] Unipolar records have disclosed absence of an initial R wave in leads from a variable portion of the wall under the endocardium; differential records have revealed instantaneous excitation and sometimes reversed excitation (epi-endocardial) in a similar part of the wall. The laboratories, the methods of leading, and the percentage of subendocardial wall thought to be instantaneously excited are as follows:

Investigator	Lead	Per Cent of Ventricular Wall Instantaneously Excited
Prinzmetal et al.[5,6]	Unipolar	50
Sodi-Pallares et al.[10]	Unipolar	66⅔
Durrer et al.[18]	Unipolar transmural, partial transmural, multiple differential	40
Scher et al.[24-27]	Multiple differential	(Close to zero)

Later experiments by the first two groups listed have led to their reducing their original estimates somewhat. In general, the results have been interpreted to mean that Purkinje fibers extend out into the wall, although this has never been demonstrated anatomically in the human heart. The results have also been projected somewhat prematurely to the clinical interpretation that only the outer portions of the ventricular wall contribute to the R wave in an epicardial or semidirect lead and that therefore subendocardial infarction can occur without electrocardiographic manifestations. There appears to be much evidence in infarction to refute this concept.[31,32] The fact that an *occasional* heart may be found at necropsy with subendocardical infarction in the absence of prior electrocardiographic abnormalities is no argument at all unless frequent (every few hours) records were made from the time of onset of symptoms until death and unless a preinfarction record was available. The readiness with which an almost monophasic record can be produced by pressure of an intracardiac electrode on the endocardium leaves no doubt about the normal electrical behavior of subendocardial muscle, varying *in no way* from other myocardium.[16] Any difference must be ascribed to factors other than the intrinsic electrical properties of the involved cellular membranes (Chapter 12, fig. [illegible]).

It is quite apparent that unipolar leads made with a recording instrument of low frequency characteristics are *not* of much use in such an experiment. Differential leads used with high frequency end instruments (C.R. tube) and good techniques have yielded *different* results.[18,26-29] The experiment on intramural leads is difficult to do, and obviously the *relation* of the myocardium to the leads varies with systole. Contraction results in considerable thickening of the wall, which alters the diastolic relationships of subendocardial and subepicardial muscle, a circumstance which possibly affects the last part of QRS. As shown by Durrer,[18] the cavity potential

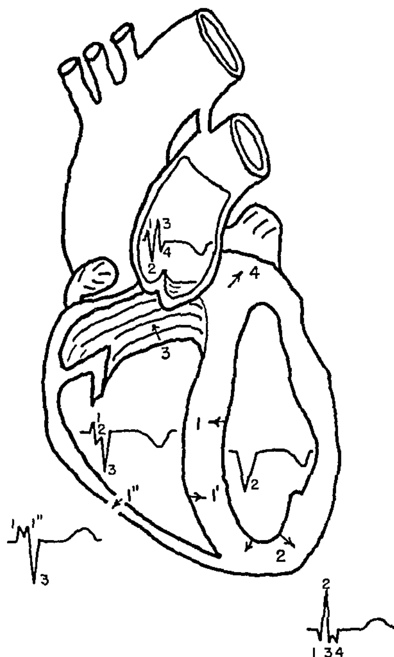


Fig 7 A schema of the human heart based on figure 5 to show one type of intraventricular conduction in the normal subject The Arabic numbers on various parts of the heart indicate relative times of excitation and correspond to the similarly numbered deflections on the form (not amplitude) of the unipolar lead from the sites indicated Notches are exaggerated for clarity Variations in normal intraventricular conduction based on differences in sequence of excitation of the ventricle are discussed in detail in Chapter 10

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Investigator	Leads	Per Cent of Ventricular Wall Instantaneously Excited
Prinzmetal et al[23, 24]	Unipolar	80
Sodi Pallares et al[3]	Unipolar	$66^2/_3$
Durrer et al[4]	Unipolar transmural partial transmural multiple differential	40
Scher et al[10-15]	Multiple differential	(Close to zero)

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being large and early, dominates the potential of the free left ventricular wall, positivity near the electrode may be simply a notch or slur on the descending limb of the cavity potential, which accounts for the small R waves in the intramural leads. None of the investigators has given any consideration to the interpretation of his results in terms of the different conductivities of the media involved—blood, myocardial wall and air—since the experiments are usually done on the exposed heart. In the case of the Prinzmetal group, the application of the method of images (Chapter 12) to the interpretation of S-T displacements of different directions on either side of the heart and absence of it in the cavity when injury has been produced in the wall seems to have been overlooked.[5]

Epicardial Leads

Epicardial leads in man have been recorded infrequently[33-35, 37] since Barker, Macleod, and Alexander[36] made their observations in a case of seropurulent (streptococcus viridans) pericarditis with pericardiostomy. In general the data obtained support the original contention that precordial leads are semidirect leads simulating in form, for the most part, the direct epicardial leads. Further, in right ventricular hypertrophy the right ventricular epicardial lead is characterized by a tall, late R wave although on selected areas of the chamber an occasional rS deflection will be found.[34] Somewhat contrary data in right ventricular hypertrophy in ten cases of tetralogy of Fallot have been obtained by McGregor.[35] In all of these, epicardial leads from the right ventricle yielded an rS configuration, and from the left a qR. The author felt that an explanation such as unusual "electrical" rotation of the heart suggested by Kossmann and associates[11] could account for the latter type of complexes in right precordial leads. It certainly appears that not enough carefully collected data on epicardial leads in man are available and that investigations along this line should be useful in answering many vexing questions on the spread of excitation in the human ventricle.

Summary

With regard to the spread of excitation in the human ventricle it seems probable that some differences exist from the description given by Lewis originally, particularly with regard to the relative amounts of the septum excited from either side and the amount excited from below upward. The available data on intramural leads is so variable that conclusions based on the absence or diminutive size of the R wave in subendocardial leads must at best be tentative. It seems that some data on injury phenomena have been erroneously interpreted because of inadequate consideration of the existence of electric images in the experiments as done.

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10 Intraventricular Conduction

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CERTAIN PECULIARITIES of intraventricular conduction previously interpreted as grades of bundle branch block and often regarded as being synonymous with heart disease can be demonstrated to occur frequently in the electrocardiograms of normal subjects Paradoxically normal intraventricular conduction as implied by classic concepts occurs rarely in healthy young subjects but is often present in older subjects who have or are suspected of having heart disease

In 1947 Wilson[1] pointed out that the thirty five years following the recognition of bundle branch block were years of endless confusion no sooner was one source of confusion eliminated than another arose From the original description by Eppinger and Rothberger[2] in 1910 until the brilliant studies of Barker[3, 4] the electrocardiographic entities now ascribed to right and left bundle branch block were erroneously interchanged

Considerable disagreement persists concerning the differentiation and clinical significance of the various types of intraventricular conduction Recognition of these types depends upon certain characteristics in the form and the duration of the QRS complex Only when the abnormal forms are accompanied by other evidence of heart disease do they have any bearing upon the clinical diagnosis So-called defects in intraventricular conduction have no effect upon the mechanical efficiency of the heart and frequently they have no correlation with the character of the cardiac and vascular pulsations which they seem to suggest[5] Therefore when considered as isolated deviations from the normal these electrocardiographic peculiarities have no clinical significance[1]

Our knowledge of the different types of intraventricular conduction arises mainly from studies of bundle branch block by two methods In the first a correlation of the form of the QRS deflections from sites within and upon the ventricular myocardium is made with deflections recorded from the body surface and limbs in experimental animals In the second observations are made during cardiac catheterization and during surgical exposure of the hearts of humans A third and less precise method is a correlative study of clinical electrocardiograms and the findings at necropsy

Information concerning intraventricular conduction in the normal human heart is limited Few studies are available in which a sufficient number of exploratory and monitor controlled leads have been used to

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establish an adequate basis for the understanding of conductive anomalies. Most investigations of normal subjects have been carried out with relatively insensitive instruments and the small but significant initial portion of the QRS complex has been poorly recorded.

In animal experiments, as well as in clinical studies, simultaneous monitor leads have not always been used to provide an accurate reference between leads with different positional relations to the heart in order to identify accurately the order of ventricular activation.

Little is known concerning the influence of normal variations in the conduction system of the heart on the electrocardiogram. However, it seems reasonable to expect as great individual variations in these structures and in their functions as in other organs.

In view of the preceding, it should be apparent that any presentation of intraventricular conduction can at best be only an arbitrary and oversimplified presentation of a complex subject. An extensive review of the pertinent literature prior to 1950 was reported by Rosenman, Pick and Katz.[6] In this chapter, the general concepts of Wilson and his associates and subsequent observations that seem to be of importance will be considered.

Methods and Materials

The majority of the electrocardiograms reproduced in this article were recorded by a Sanborn Twin Beam Cardiette Model 62 with a flat frequency response to 500 cycles per second. Each limb of the Wilson central terminal contained a resistor of 100 000 ohms, while the internal resistance of the electrocardiograph was 5 megohm. Unipolar extremity leads rather than augmented extremity leads were employed. A right sided unipolar chest or extremity lead was used as a monitor lead because in most instances such a lead provided the earliest evidence of the onset of ventricular activation. A paper speed of 75 mm per sec and twice normal standardization of the galvanometers (1 mv = 2 cm) were employed.

The vectorcardiograms were recorded with a Sanborn Vector System standardized so that 1 mv produced a 2 inch deflection or a 10 inch deflection.

Bipolar limb, unipolar limb and unipolar esophageal leads were recorded in the conventional fashion. Unipolar chest leads from the conventional and other sites on the chest were recorded. Sites at conventional position but on the right side of the chest are designated by an apostrophe following the symbol V rather than by the customary subscript R, i.e., $V'_3 = V_{3R}$. Unipolar chest leads from high sites are designated by a numerical prefix indicating the level with reference to an intercostal space at the sternal junction. Thus $_2V_2$ indicates a position in the second intercostal space above the conventional chest site V_2.

The young healthy subjects studied ranged in age from 17 to 40 years. They had no evidence of heart disease by history or physical examination and did not display an unusual shape or size of the cardiac silhouette on fluoroscopic examination. The older subjects (40 years and above) with heart disease or suspected heart disease were studied as in patients or out patients on the Fourth (N. Y. U.) Medical Division, Bellevue Hospital.

Right sided catheterization was performed by the conventional venous approach Left sided catheterization was by the direct posterior transthoracic approach

SEQUENTIAL TYPES OF INTRAVENTRICULAR CONDUCTION

There are at least four common, fundamental types of intraventricular activation recognizable in both healthy[14] and pathologic states[28] It is impossible both at the present time and in the foreseeable future to define with accuracy the dividing line between physiologic and pathologic forms unless changes have been observed to develop in the serial electrocardiograms of any one subject that can be correlated with certainty with other objective manifestations of heart disease

In view of the above considerations and the implied limitations of conventional nomenclature for intraventricular conduction a more general and encompassing classification[20] will be used in this chapter This classification does not differentiate between physiologic and pathologic variations but is purely descriptive of the *sequence* of ventricular excitation It is as applicable to vectorcardiography as to electocardiography

The terminology for the four basic forms to be used subsequently is (1) *initial left septal–late left mural actuation* the classic normal type of intraventricular conduction (2) *initial left septal–late right mural actuation* in which excitation of the right ventricular free wall is delayed relative to that in the previous type and in which the form of the latter portions of the QRS complex simulates various degrees of right bundle branch block (3) *initial right septal–late left mural actuation* in which excitation of the left side of the interventricular septum occurs later than excitation of the right side and in which the form of the initial portions of QRS simulate left bundle branch block (4) *initial right septal–late right mural actuation* with combined features of the previous two types previously designated as bilateral incomplete bundle branch block

Initial Left Septal–Late Left Mural Actuation *(Classic Normal Intraventricular Conduction)*

The concept of normal intraventricular conduction introduced by Lewis and Rothschild[7] in 1915 and later modified by Wilson and associates[1,3,9] has been followed or implied in most textbooks and by most investigators[6,10] Although as already indicated there are reasons to suspect that this type of ventricular activation implied by the form of the electrocardiogram is present in only a small percentage of healthy young adults[11,14] this concept will nevertheless be used to represent an idealized or classic normal because it is the simplest type of intraventricular conduction and one from which a beginning may be made most easily

Evidence supporting Wilson's modification of the Lewis and Rothschild

concept of normal intraventricular conduction is based upon concordant data from investigations on experimental animals[7, 9, 17] and on humans.[10, 14, 18, 19] In all these studies, it is theorized that excitation is delivered from the atria to the ventricles by way of the specialized conduction system consisting of the A-V node, the bundle of His, the right and left bundle branches, and the Purkinje tissue. Although direct proof of atrioventricular conduction by this pathway is not available, strong *inferential evidence of A-V conduction by these specialized tissues is to* be found in many animal studies. Small cuts properly placed on the right and left upper sides of the septum cause characteristic changes in the ventricular complex consistent with an interruption of such conduction pathways.

The first phase of ventricular activation results from delivery of the excitation impulse by the left bundle branch to the subendocardial Purkinje plexus to the midportion of the left interventricular septum.[17, 18] The presumably longer right branch delivers its impulse to the subendocardium of the right septum a fraction of a second later. The delayed activation of the right septum, relative to that of the left side, is the basis for Wilson's considering that "a very minor grade of incomplete right bundle branch block, then, is physiologic."[1]

The interventricular septum is generally regarded to consist predominately of left ventricular muscle mass and, to a lesser extent, of right ventricular muscle mass. The rightward directed activation process in the more massive left septal muscle produces electrical forces of much greater magnitude than those from the relatively delayed leftward directed process of shorter duration in the thin right septal muscle. The initial greater forces from the left septum completely overbalance those from the right septum. Thus the resultant electrical manifestation of the septum as a whole is dominated by the left septum and is indicated by vector 1 of figure 1. The initial negative QRS deflection in leads from the left cavity and free wall, and the positive deflection in leads from the right cavity and free wall, are due to the septal forces.[7, 9, 17, 19]

The free walls of the ventricles have long been considered to be activated in an endo-epicardial direction,[7, 9] despite certain observations to the contrary.[0, 3] Since recent evidence acquired by means of excellent techniques supports the original concept,[17] it is the one that will be accepted for this presentation. Vector 2 of figure 1 represents the strong and rapid development of forces directed from endocardium to epicardium in the left ventricular free wall.

Activation of the thin right ventricular free wall begins after and is completed before that of the thick left ventricle[17] and is represented by vector 4 of figure 1. According to Wilson,[1] the instant of activation of

the ventricular epicardium beneath a unipolar chest lead is indicated by a point at the end of the intrinsic deflection and not at its beginning.' The intrinsic point is located on the R wave as it descends to or crosses the baseline. However, in this simplest type of ventricular activation the electrical forces of the normal thin right ventricular free wall cannot be recognized as a characteristic QRS deflection in clinical electrocardiograms. The observations of Barker and Valencia[15] substantiate this concept. They demonstrated that when normal intraventricular conduction alternates with complete right bundle branch block, the initial QRS deflection is similar in all leads with normal conduction or with right bundle branch block. This is illustrated in the electrocardiograms reproduced in figure 2. Also simultaneous unipolar right ventricular cavity and precordial leads in the presence of normal ventricular activation have identical intrinsic points.[15]

The early, rapid, large forces in the free wall of the left ventricle counterbalance the individual manifestations from the right ventricular free wall. Therefore the concept of the intrinsic point is an indication in right precordial leads of the time at which the underlying right ventricular

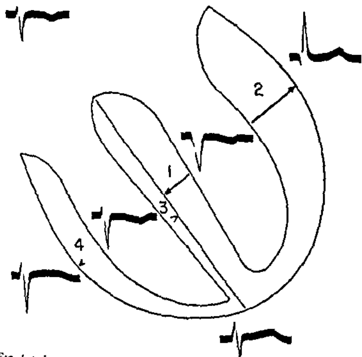


FIG 1. Schema of classical normal intraventricular conduction (initial left septal—late left mural activation)

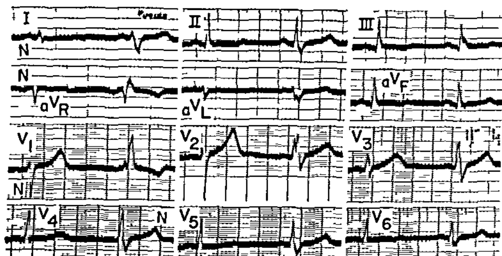


Fig 2 Transient complete right bundle branch block The first complex of each pair represents classical normal intraventricular conduction the second complete right bundle branch block The patient was a 39 year old man without symptoms or signs of heart disease (From Wilson et al Advances in Internal Medicine 1947 fig 11 [1])

epicardium is activated is not applicable when this type of intraventricular conduction is present Further conduction of this type can be reduced to two vectors, the first being the resultant of the right and left septal forces, and the second the resultant of the forces from the right and left ventricular free walls

*In view of the complexities that arise in discussing other types of intra*ventricular conduction and the desirability of a common frame of reference for purposes of communication a scheme of ventricular conduction, represented by figure 3 is convenient Vector symbols and drawings of simultaneous deflections are used in figure 3 to indicate the hypothesized sequence of ventricular activation

Characteristics of the isolated right and left septal forces respectively are suggested by the initial QRS deflection in unipolar leads from the right cavity when left or right bundle branch block is present [18, 4] The isolated rightward directed left septal forces (vector 1) are represented by the negative deflection (LS) of figure 3 as would be recorded by a unipolar lead on the left side of the septum These forces are responsible for the initial negativity of the left cavity (LC of fig 3) and precordial (LP) unipolar leads The initial positivity of the right cavity (RC) and precordial (RP) leads are due to the same forces The isolated leftwardly directed right septal forces (RS and vector 3) are indicated by a small positive deflection, as *would be recorded by a unipolar lead to the left of the inter*ventricular septum The resultant of the right and left septal forces, re



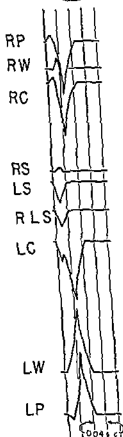


FIG 3

FIG 4

FIG 3 Schema of classical normal intraventricular conduction RP right precordial lead RW right ventricular free wall electrogram RC right cavity lead RS right septal electrogram LS left septal electrogram R LS total septal electrogram LC left cavity lead LW left ventricular free wall electrogram LP left precordial lead

FIG 4 Classical normal type of intraventricular conduction Male patient age 47 hypertensive cardiovascular disease with a five year history of congestive heart failure

corded in a unipolar lead to the left of the septum, is represented by a negative deflection (R I S).

Activation of the free left ventricular wall (vector 2) begins very nearly at the same time as, or immediately after, the beginning of left septal activation and continues throughout the remainder of the QRS interval.[17] The isolated endocardial to epicardial forces of the free wall are represented by the positive deflection (LW), as would be recorded in a unipolar lead near the left ventricular epicardium. These forces are responsible for the positive deflection in the left precordial leads (LP), for part of the negative deflection in the left cavity (LC), and for all of the negative deflections in the right cavity (RC) and right precordial (RP) leads.

The forces of the thin right ventricular free wall (vector 4) are presumably counterbalanced by the early and rapid development of strong forces in *the left ventricular free wall. The character of the former can be inferred* from findings in incomplete right and complete left bundle branch block.[19] In some minor degrees of incomplete right bundle branch block in which right mural activation occurs after the phase of strongest left ventricular excitation, the small secondary R wave in unipolar right chest leads represents in nearly pure form the isolated forces of the right ventricular free wall.[19] The same forces are thought to cause the small R wave in unipolar right precordial leads with complete left bundle branch block when unipolar right cavity leads do not demonstrate an upward deflection during this phase of the QRS.[19, 4] The isolated forces of the right ventricular free wall (vector 4) with normal intraventricular activation are indicated in figure 3 by a small upward deflection (RW) beginning shortly after the onsets of left and right septal excitation and during the increasing *phase of left mural activity.*

In clinical electrocardiograms suggesting the type of normal intraventricular conduction under consideration and shown diagrammatically in figure 3 the QRS interval in precordial leads is 0.10 to 0.12 sec in duration.[14] In limb leads, where the initial and final portions of the QRS complex are less easily recognized, the QRS interval appears to be shorter. The electrocardiograms reproduced in figure 4 are those of a 47 year old male with long standing arterial hypertension and chronic congestive heart failure of five years' duration. These tracings are typical of the classic type of intraventricular conduction. The form of the QRS complex in the leads reproduced here, as well as those from numerous other chest sites, suggest that the idealized normal type of intraventricular conduction is present. The absence of secondary R waves in lead V_R and in right chest leads, *and the absence of S waves in leads opposite* the left ventricular epicardium permits this type of intraventricular activation to be represented

by two main vectors As already noted the first is the resultant of the septal forces and the second the resultant of the forces of the right and left free ventricular walls

It is interesting that electrocardiograms of this type indicating initial left septal and late left mural activation were used to represent the normal in several publications by Wilson[1, 8, 25] This type of electrocardiogram is relatively rare in subjects below 40 years of age without heart disease[14] but occurs frequently in patients over 40 who have or are suspected of having heart disease Although this concept of the sequence of intraventricular activation has long been regarded as characteristically representative of the normal there is little clinical data to substantiate this point of view

In 1943 Gardberg and Ashman,[27] after analyzing clinical electrocardiograms suggested that final ventricular activation in normal subjects characteristically takes place in the base of the septum or of the right ventricle Subsequently Groedel and Borchart[3] recorded electrocardiograms directly from pericardial sites in a few subjects without heart disease compatible with this concept

Kossmann and associates[9] observed late secondary R waves in leads from the right ventricular outflow tract of normal subjects suggestive of late activation of the crista supraventricularis Recent clinical studies[11, 14] further indicate that in the majority of healthy young subjects final activation occurs in the base of the septum or of the right ventricle Scher and Young[7] have demonstrated by direct intramural leads that final ventricular excitation in presumably normal dogs is located in the base of the interventricular septum

The clinical evidence suggesting that final ventricular activation in the majority of healthy young subjects occurs in the base of the septum or of the right free wall is the presence of late secondary R waves in the unipolar right arm and right chest leads[11, 1, 14, 16] The final and unbalanced forces of activation are usually directed anteriorly upward and to the right This type of intraventricular conduction with initial left septal and late right mural activation is at the present time indistinguishable from or identical with certain types of incomplete right bundle branch block as defined by Barker and Valencia[19]

Intraventricular Block

The term intraventricular block usually implies that a delay is present in activation of some portion of the ventricles of such degree as to prolong beyond certain limits the total duration of excitation However conditions in which an unusual *sequence* rather than a prolongation of total ventricular

activation occurs are often included in this classification, as indicated above Paradoxically, with certain minor aberrations of conduction to the left ventricle the QRS interval may actually be shortened

In general, two main types of defects in intraventricular conduction are recognized and are ascribed to a delay of or an altered sequence of excitation to some part of the ventricles The first presumably involves the main branches of the bundle of His and is called bundle branch block In the second, the defect is considered to be located distal to the bundle branches and is designated by various investigators as "arborization" "focal" "parietal," "muscle fiber," "peri infarction" etc, block The second is not as clear cut as the first, and differentiation between the two is often clinically impossible A third type of intraventricular conduction sometimes classified as a block is anomalous atrioventricular excitation (Wolf Parkinson White syndrome) in which some part of the ventricles is activated prematurely in comparison to the usual sequence of A V conduction

Delay in conduction through the right or left bundle branch may occur unilaterally or bilaterally in varying gradations The degree of the delay ranges from the difficult to define incomplete to the more easily recognized complete bundle branch block If the block is complete in both bundles then complete A V block must occur unless an accessory atrioventricular conduction pathway is present [30]

The delay in bundle branch conduction may be constant or inconstant Its presence may be determined by the sinus rate With slow rates the block may be absent with faster rates either complete bundle branch block or intermediate grades of block directly related to the rate may appear [6] The term partial bundle branch block also called intermittent bundle branch block indicates a condition analogous to that of partial A V block when the defect in conduction comes and goes or the degree of block varies in the course of one electrocardiographic recording

Incomplete block in one bundle and complete block in the other bundle has been presumed in retrospect when conduction in the completely blocked branch returns to normal and allows recognition of the contralateral incomplete block [31] Also alternation of various degrees of right and left bundle branch block in the same individual have been described [32]

Bilateral incomplete bundle branch block has been suggested as a recognizable entity when electrocardiographic findings demonstrating characteristics of both incomplete right and incomplete left bundle branch block are concomitantly present [33]

Certain arbitrary and empiric criteria concerning the form and duration of the QRS complex are conventionally used to define gradations of unilateral bundle branch block However these criteria differ from one authority to another [6] By general conventional standards incomplete bundle-

branch block requires in addition to certain characteristic forms of the initial ventricular complex a QRS interval less than 0 12 sec in duration Theoretically incomplete bundle branch block can be divided into low grade and high grade types depending on the degree of temporal asym metry of ventricular excitation

The conventional criteria for complete bundle branch block require that the QRS interval measure 0 12 sec or longer These values for the QRS interval in bundle branch block are to a great degree arbitrary and have in part been established from animal studies Complete bundle branch block can only be recognized with absolute certainty under ex perimental conditions by severance of the contralateral bundle branch to produce complete A V block There are few clinical situations in which absolute evidence of the completeness of bundle branch block can be recognized

The specific types of bundle branch block are most conveniently pre sented by discussing the more clear cut complete blocks first and then the lesser degrees

Initial Left Septal–Late Right Mural Activation *(Right Bundle Branch Block Type)*

Complete right bundle branch block implies that the left ventricular septal mass and the free wall are activated as in the classic normal type of con duction and that the right ventricular septum and free wall are activated by a delayed and anomalous mechanism

In figure 5 the electrical forces of the left septal mass are indicated by the first vector The loss of the relatively small forces from the normal activation of the thin right septal mass during this phase is apparently so insignificant as to be unrecognizable in the clinical electrocardiogram (refs 18 and 19 and fig 2) Thus the initial portion of the QRS complex is not appreciably different from what is found in the classic type of intra ventricular conduction The second vector represents the forces of activa tion in the free wall of the left ventricle

After the onset and perhaps during excitation of the left ventricular wall anomalous activation of the right ventricular septal mass occurs in a left to right direction (vector 3) The latter forces are relatively weak and their counterbalancing effects on the stronger left mural forces are small Therefore the anomalously excited right septum causes only a slight reduction in amplitude of the R wave in the left precordial leads In right cavity leads the delayed anomalous activation of the right septal mass is responsible for a conspicuous upward or slurred deflection following the positive deflection due to left septal forces[9, 18, 19, 33] Deflections re sulting from such anomalous septal excitation are prominently demon

strated in the leads from the apex of the right cavity in figure 6 The greater magnitude and duration of forces from anomalous left to right activation of the thin right septum than from normal activation in the opposite direction implies the presence of a fundamentally different type of myocardial conduction in the two types They suggest that more of a series like (in an electrical sense), slow, direct muscle conduction occurs with anomalous excitation in contrast to the parallel like (in an electrical sense) and more rapid excitation with normal conduction Precordial leads opposite the free wall of the right ventricle do not, as a rule demonstrate easily recognized evidence of delayed right septal forces This may be due in part to the counterbalancing effect of the stronger forces from the left ventricular free wall on the right precordial site, or it may be because the deflections seen in the cavity leads are fused in the right precordial *leads with the effect of forces arising in the free wall of the right ventricle*

As a result of direct intramural electrocardiographic observations in dogs, Sodi Pallares [3] has suggested that with complete bundle branch

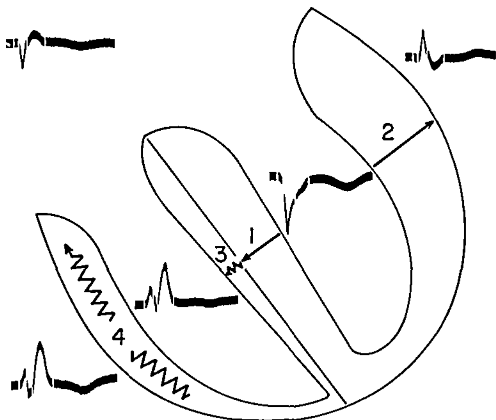


Fig 5 Schema of complete right bundle branch block (initial left septal—late right mural activation)

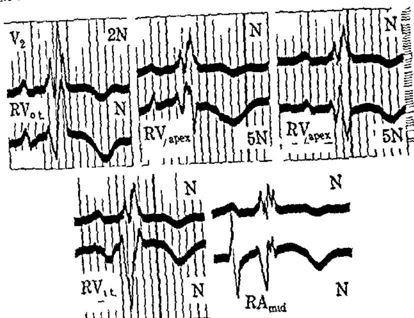


FIG 6 Precordial and right cavity leads with complete right bundle branch block o.t. outflow tract, i.t. inflow tract

block there is an exceptionally long delay i.e. 0.04 sec in passage of the excitation process from the normally activated septal mass across the septal junction ("physiologic barrier") to the contralateral septal mass. He believes that this delay in passage from the septum of one ventricle to that of the other accounts for most of the prolongation of the QRS interval in complete bundle branch block. Erickson and associates[11] in similar studies but employing a more elaborate technique have presented data consistent with a uniform spread of excitation from the side of the intact bundle branch to the contralateral septum without unusual delay at the site of the interseptal junction. The observations of the latter are more consistent with the findings in leads from the right ventricular cavity with complete right bundle branch block in man.

Unipolar leads from some sites within the right ventricular cavity[18] demonstrate the onset of anomalous left to right activation of the right septum before the deflection representing left septal activation can descend to the baseline. Therefore, although the findings in right cavity leads indicate a delay in onset and spread of activation to the right septum, it is not evident in all cases that an unusual delay occurs in spread of the excitation wave across the interseptal junction.

The free wall of the right ventricle is activated late. The onset probably

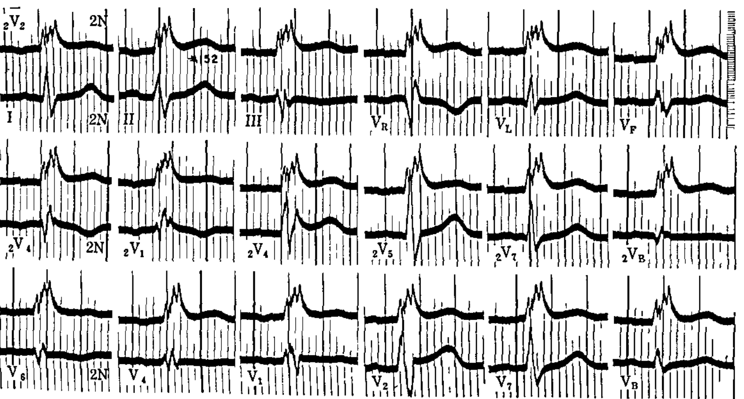


Fig 7 Complete right bundle branch block Thirty four year old healthy male physician

begins shortly after that of the anomalous left to right excitation of the right septum A great deal of confusion exists concerning the exact course of activation in the free wall on the side of the bundle branch block. As a result of animal studies with direct lead Sodi Pallares[7, 3] has suggested that the free wall of the affected ventricle is activated in the same endocardial to epicardial sequence and speed as with normal intraventricular conduction Erickson[38] has performed similar experiments and interprets his findings as indicating abnormalities in both the sequence and duration of ventricular free wall activation on the affected side Erickson's conclusions are in agreement with opinions from Wilson's laboratory [19]

In some instances of complete right bundle branch block simultaneous, right ventricular cavity and overlying precordial leads show nearly identical late positive deflections of long duration (ref 18, see fig 6) This observation is consistent with an abnormal order of activation in the right ventricular free wall with an apex to base direction that is predominantly parallel to the endocardial and epicardial surfaces The prolonged duration of the right endocardial and epicardial secondary R wave is also more consistent with slow muscle conduction than with excitation through the fast conducting Purkinje network This concept of anomalous right mural activation with complete right bundle branch block is indicated in figure 8 by vector 4 The slurred final S wave in leads opposite the left ventricular free wall also originates from this vector

The electrocardiograms of figure 7 demonstrating right bundle branch block with a QRS interval of 0 16 sec are those of a 34 year old healthy male physician

The schema in figure 8 indicates the theoretical relationship between the classic type of normal conduction with initial left septal and late left mural activation (column 7) and complete right bundle branch block (column 1) Left septal and free wall activation are responsible for the same deflections in right bundle branch block as with normal conduction Delayed anomalous right septal activation (vector 3 column 1) following the cessation of left septal excitation (vector 1) produced a right septal (Rs) deflection of greater duration and magnitude and is opposite in direction to that seen with normal right septal activation Anomalous right septal forces produce a conspicuous positive deflection in leads from some right cavity sites when the exploring electrode is presumably close to the site of septal activity while in leads at other right intracavitary locations such deflections may be small or absent Some right precordial sites may show identical deflections as those from the right cavity both representing anomalous right septal excitation However these deflections vary as much from one right precordial site to another as do those from different sites within the cavity In the right precordial (RP) lead rep

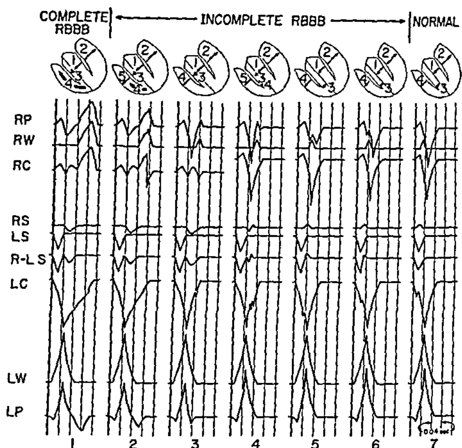


Fig. 8 Schema representing progressive gradations of incomplete right bundle branch block between classical normal intraventricular conduction and complete right bundle branch block. Symbols the same as for figure 3.

resented in column 1 of figure 8 the right septal (RS) deflection is represented as being fused with the upward deflection due to activation of the free wall of the right ventricle. Presumably the oppositely directed forces of the left ventricular free wall, because of their relatively greater strength, may be responsible for a downward notch or negative deflection in the QRS complex of right cavity and precordial leads. In general, cavity leads with complete right bundle branch block show broader and taller late R waves from sites close to the base than from sites near the apex of the right ventricle. Also, late R waves may be absent and deep S waves present in apical intracavitary leads. Great variations occur in the form of right precordial and cavity leads in complete right bundle branch block not only as the result of slight differences in electrode sites but because of variations in the counterbalancing effects of oppositely directed forces in the left free wall.

Incomplete right bundle branch block implies that the right branch is

functioning but that arrival of its impulse in the right ventricle is delayed even more, relative to left septal activation, than with so-called normal conduction There are as many possible gradations of incompleteness or delay in right bundle branch conduction as in atrioventricular conduction

Low-grade incomplete right bundle-branch block of a minor degree is represented in column 6 of figure 8 The delay in onset of right septal activation is indicated by the slightly later appearance of the right septal (RS) deflection than with normal conduction

Electrocardiograms illustrating this type of conduction are reproduced in figure 9 They are from a 59 year old man without evidence of heart disease The arterial blood pressure was 120/80 mm Hg The secondary R wave in lead V_R and the small upward notch in the S wave of leads V_1 and $_2V_2$ suggest delayed rightward activation of some part of the right mural myocardium The absence of a simultaneous upward deflection in the lead from the right ventricular outflow tract lends support to the presence of an endocardial to epicardial activation of the right ventricular free wall

Column 5 of figure 8 represents a slightly greater degree of low grade incomplete right bundle branch block Activation of the septal and free ventricular walls occurs in the same fashion as in normal conduction However right septal activation relative to left septal activation is still further delayed

As will be demonstrated later it is believed that both low grade incomplete bundle branch block as well as minor degrees of high grade incomplete bundle branch block do not necessarily represent true blocks in bundle branch conduction

High-grade incomplete right bundle branch block can be considered when a portion of the right septum is anomalously activated as a result of the left septal impulse crossing the interseptal junction Column 4 figure 8 illustrates partial initial anomalous activation of the right septal mass (vector 3) and final right septal excitation (vector 4) from the right bundle impulse Thus *partial anomalous* rightward activation of the right septum is designated by *a late extension of the left septal* vector (vector 1 column 4) crossing the interseptal junction into the right septum (vector 3 column 4) This force is represented by the initial downward deflection in the isolated right septal electrocardiogram (RS) The leftward right septal forces (vector 4 *column 4*) are represented by a small late positive deflection in the isolated right septal electrocardiogram (RS) *In* this grade of incomplete right bundle branch block the vectors and deflections representing the *forces of left* ventricular septal and mural activation are unchanged *from* those with normal conduction

The delayed but normally directed *endo* epicardial forces of the right



Fig 9 Minor degree of low grade incomplete right bundle branch block Male patient age 59 without symptoms or signs of heart disease Note upward notch in S waves of leads V_1 and $_2V_2$ and absence of similar findings in right ventricular cavity lead

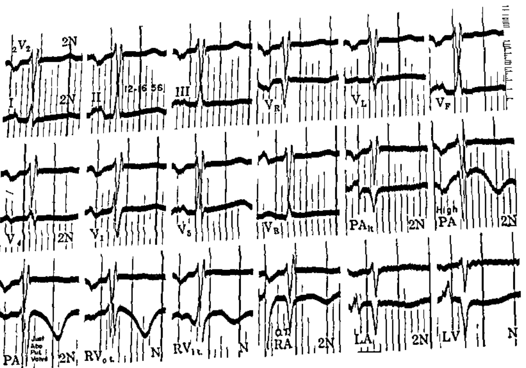


Fig 10 High grade in complete right bundle branch block Female patient age 31 with tight mitral stenosis (confirmed by surgery) and congestive heart failure Secondary R wave in lead from right ventricular outflow tract (o t) suggests anomalous right septal activation See ondary R wave in lead $_2V_2$ occurs later than those in right ventricular cavity lead and suggests delayed activation of the right ventricular free wall

ventricular free wall (vector 5, column 4) are indicated by the upward deflection in the theoretically isolated, right wall electrogram (RW) and the secondary R wave (or upward deflection) in the unipolar right precordial lead (RP). They are drawn as occurring later in the QRS interval than with normal ventricular activation (column 7, figure 8) or with lesser degrees of incomplete right bundle branch block (columns 5 and 6) and after the phase of most rapid and strongest, left ventricular excitation. Further, they are completed before the end of left ventricular activity.

Figure 10 is a reproduction of electrocardiograms illustrating this type of conduction. They are of a 31 year old woman with tight mitral stenosis, confirmed by surgery, and congestive heart failure. Resting blood pressure values were: pulmonary artery 80/45, right ventricle 80/8, left ventricle 105/12 and left atrium 35 mm Hg.

Overy and Johnston[34] have suggested that in subjects without heart disease, secondary R waves may occur in high right chest leads but are *absent in lateral right chest leads. However, in a series of 100 young,* healthy adults, Sud and Bryant[14] found secondary R waves in right lateral chest leads at the level of the fourth and fifth intercostal spaces in 73 per cent of these subjects.

The electrocardiograms reproduced in figure 11 are those of a 25 year old healthy, male physician. These electrocardiograms are compatible with high grade, incomplete right bundle branch block as represented in column 4 of figure 8. The longest QRS interval in precordial leads is 0.09 sec. Secondary R waves suggestive of late activation of some part of the right ventricular free wall or of the base of the septum are present in leads V_R, $_2V'_R$ V'_6, $_2V$ V'_6 and V_1.

Secondary R waves are present in lead V_R in 95 per cent of young, healthy subjects showing similar deflections in leads from the right chest.[14] None of the subjects without secondary R waves in right chest leads showed true secondary R waves in lead V_R.[14] Therefore, in contrast to the opinion of Barker and Valencia,[19] secondary R waves in the unipolar right arm leads would seem to be a highly reliable indication of so called incomplete right bundle branch block.

A still greater degree of incomplete right bundle branch block is represented in column 3 of fig. 8. Again activation of the left septal mass and the right wall occurs as in the normal (column 7) and in lesser grades of incomplete right bundle branch block (columns 4, 5 and 6). Right septal activation is entirely anomalous with a left to right direction (vector 3, column 3). The anomalous right septal forces produce a relatively large negative deflection of great duration in the isolated right septal (RS) electrogram, and a second upward deflection in the unipolar right cavity lead (RC). Some of the manifestations of the anomalous right septal

forces in the right cavity may be counterbalanced by activity in the left ventricular free wall (vector 2 column 3) The final portion of the initial R wave and some part of the secondary R wave in the unipolar right precordial (RP) lead may also be due to these anomalous right septal forces

As long as the delay in right ventricular activation is of a slight degree, the free wall of the right ventricle is presumed to be excited with the same endocardial to epicardial direction and speed as in normal intraventricular conduction (column 7 fig 8) and the lesser degrees of incomplete right bundle branch block (columns 4 5 and 6) Therefore there is no reason to suppose that the true magnitude of the forces in the free wall of the right ventricle in those gradations of incomplete right bundle branch block with a presumably normal sequence of free wall activation differ from those with normal ventricular excitation[19] However there is every reason to suppose that the magnitude of the forces of the right ventricular wall vary greatly from one subject to another

In the degree of incomplete right bundle branch block indicated in column 3 of figure 8 activation of the right wall continues after completion of activation of the left ventricle Thus the S wave in the left precordial lead (LP) represents late activation of the right ventricle The electrocardiograms reproduced in figure 12 of a 25 year old healthy male physician are characteristic of this degree of delay in right ventricular excitation The QRS interval is between 0 11 and 0 12 sec The secondary R waves in the right sided leads occupy the final portion of the QRS complex while left chest leads show broad slurred S waves

The studies of Erickson[22] suggest that many intermediate gradations in right branch block exist between the degree of incomplete block indicated in column 3 and the complete block in column 1 of figure 8 Thus depending upon the degree of delay in arrival of excitation from the right bundle branch varying amounts of the right ventricular free wall may be activated by the anomalous process from the left septum Column 2 of figure 8 represents a grade of incomplete right bundle branch block or delay in right ventricular excitation in which the free right wall is activated initially by the anomalous process (vector 4) and finally by the impulse from the right bundle branch (vector 5)

The electrocardiograms reproduced in figure 13 are those of a 39 year old male with advanced mitral stenosis The pulmonary artery pressure at rest was 98/52 mm Hg and the right ventricular pressure 98/23 mm Hg At autopsy moderate right ventricular hypertrophy and dilatation were found with marked calcified mitral stenosis The QRS interval is 0 09 sec and the form of the QRS complex suggests a degree of high grade incomplete right bundle branch block similar to that illustrated in column

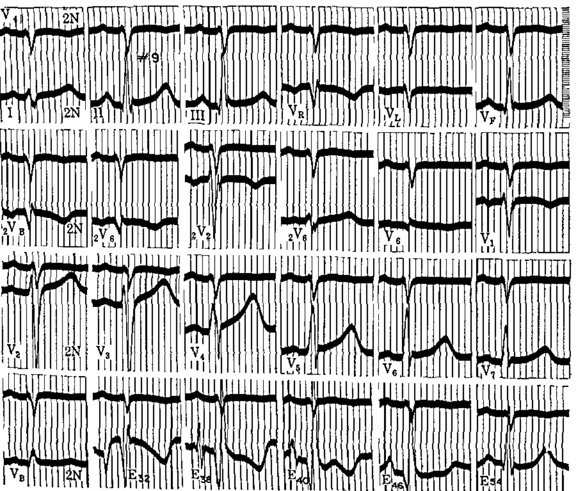


Fig 11 High grade incomplete right bundle branch block Healthy 28 year old male physician

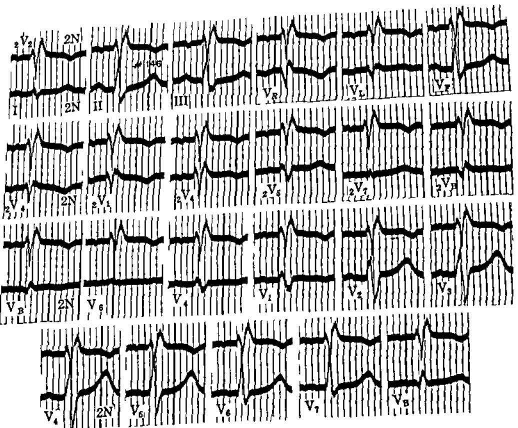


FIG 17 High grade incomplete right bundle branch block Healthy 25 year old male physician QRS interval between 0 11 and 0 12 sec

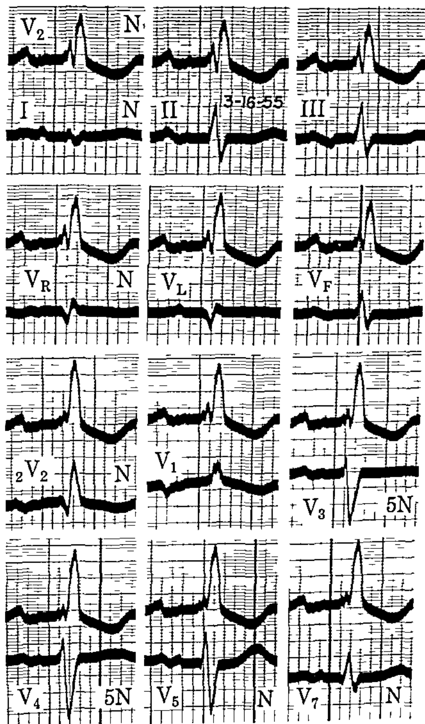


Fig 13 High grade incomplete right bundle branch block Male patient age 39 with advanced calcified mitral stenosis (autopsy confirmation) and congestive heart failure The large secondary R waves in right chest leads resemble those of figure 2

3 figure 8 Although the tall secondary R waves in right precordial leads raise the question of right ventricular hypertrophy it is believed that these may not be specifically due to hypertrophy but rather to high grade incomplete right bundle branch block (see fig 2)

Figure 14 shows the electrocardiograms of the same patient recorded

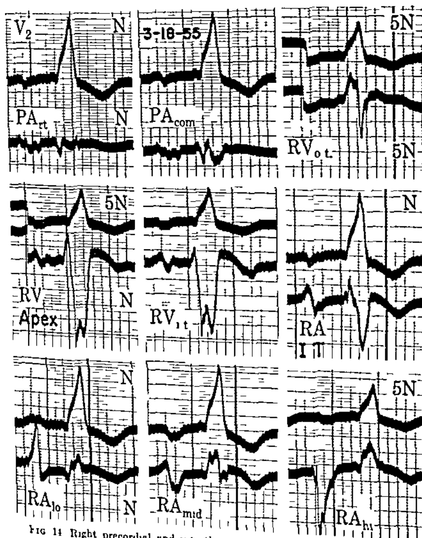


FIG 14 Right precordial and intrathoracic leads of same patient represented in figure 1 A greater degree of high grade incomplete right bundle branch block is present suggesting partial anomalous right ventricular free wall activation similar to that represented by column 2 figure 8

during right heart catheterization, when a greater delay in right bundle branch conduction was present. The QRS interval increased from 0.09 to 0.13 sec and the secondary R waves in lead V_2 had become taller and broader. In the lead recorded from the right ventricular outflow tract (just below the pulmonic valve), a prominent, rapid, negative deflection was demonstrated, 0.09 to 0.10 sec after the onset of the QRS complex and 0.01 sec before the apex of the secondary R wave in lead V_2. This rapid negative deflection from the right ventricular outflow tract area suggests that final right ventricular activation occurred in an endocardial to epicardial fashion. Thus, these electrocardiographic observations are compatible with the type of high grade, incomplete right bundle branch block indicated in column 2 of figure 8 if the assumption is valid that in complete right bundle branch block the right ventricular free wall activation is parallel to the ventricular surfaces.

Even greater degrees of what might be considered as incomplete right bundle branch block have been discussed by Rosenbaum and Lepeschkin.[31] They are instances in which right bundle branch conduction is recognizable only when complete left bundle branch block develops.

At the present time it is not possible to identify the gradations of incompleteness of right bundle branch conduction or to differentiate between high grades of incomplete and complete right bundle branch block in routine clinical electrocardiograms with any great precision. Barker and Valencia[19] suggest that complete right bundle branch block may be present when the QRS interval is less than 0.12 sec. On the other hand incomplete right bundle branch block may well be represented in the electrocardiograms of figure 14 with a QRS interval of 0.13 sec.

Relationship of Heart and Electrode Positions

In some experimental[13, 36] and clinical[6, 3] studies intraventricular conduction has been observed to change from normal through various grades of incomplete to complete right bundle branch block. It has been implied that serial changes in the QRS deflections observed in a single precordial lead of one subject, may serve as an index for recognizing the degree of a conduction defect in other subjects with fixed grades of block.[23] Inherent in such an implication is the assumption that a specific chest electrode site has the same positional relation to the heart of one patient as to that of another.

Figure 15 illustrates the variability of relations between standard chest sites V_2 and V_4 and the hearts of 103 healthy subjects with the cardiac apex as a common point of reference.[37, 38] The chest sites were identified fluoroscopically, and metal chest electrodes 2 cm in diameter were then attached. Orthodiagrams outlining the thorax, the heart and the electrodes

were drawn The cardiac apical point was identified as the junction of the longitudinal axis of the heart with the apex after the method of Ashman [29] Chest site V_2 varied 10 cm vertically and 8 cm horizontally relative to the apical point Still greater variations between conventional right precordial sites and the heart are to be expected and are observed in older patients with pulmonary emphysema or protuberant abdomens

The electrocardiograms of the healthy young male reproduced in figure 7 demonstrate that leads recorded from different right chest sites show such great variations in the form of the QRS complex as to fulfill requirements for a strict pattern type of criteria for many degrees of right bundle-branch block It therefore seems reasonable that some serial electrocardiographic changes recorded over a long period of time such as the appearance of a secondary R wave in right precordial leads may be due to changes in electrode placement or to variations in the position of the heart rather than to a change in intraventricular conduction

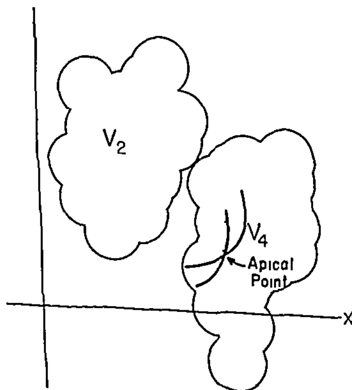


Fig 15 Diagram illustrating the variations in precordial electrode sites V_2 and V_4 relative to the apical point of the heart in 103 healthy young subjects The intersecting curved lines represent the extremes of the cardiac apical contours

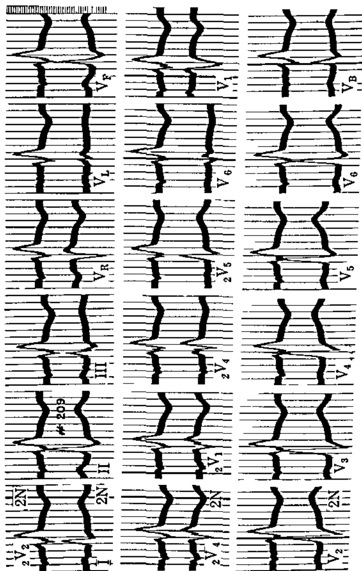


Fig 16 High grade incomplete right bundle branch block with large secondary R waves in leads $_2V_1$ through $_2V_4$ Eighteen year old healthy student nurse

Right Bundle Branch Block versus Right Ventricular Hypertrophy

The differentiation between large R waves in right precordial leads due to right ventricular hypertrophy from those due to a delay in conduction to the right ventricle presents one of the most difficult problems in electrocardiographic diagnosis

Many patients with right ventricular hypertrophy on the basis of congenital cardiovascular defects with a high right ventricular systolic pressure demonstrate tall R waves in right precordial leads similar to those seen in the electrocardiograms of newborn infants [40] On the other hand, patients with acquired cardiovascular defects and right ventricular systolic hypertension dilatation and hypertrophy display similar electrocardiographic peculiarities infrequently unless a delay in conduction on the right is also present [41]

Barker and Valencia[19] have reported the appearance of large secondary R waves in right precordial leads with the development of complete right bundle branch block in the absence of any clinical indication of right ventricular hypertrophy (fig 2) It seems probable that the electrocardiographic diagnosis of hypertrophy is specific only when in the absence of a high degree of delay in right ventricular activation the R waves in right precordial leads are taller than those in left precordial leads Hypertrophy in the presence of a major degree of incomplete right bundle branch block can be inferred with little certainty from the electrocardiogram *If the* wall activation on the right is sufficiently delayed as to follow the phase in which maximal forces are developed in the left free wall excitation of the former alone can in some instances account for relatively tall secondary R waves in right chest leads (figs 2 6 7 12 16 and 21)

The so-called delay of the intrinsic point in right precordial leads has been regarded by some authorities as evidence of right ventricular hypertrophy In our opinion this apparent delay in the intrinsic point is more often due to the anomalous right septal force of unrecognized incomplete right bundle branch block than to right ventricular hypertrophy [9]

Figure 16 shows the electrocardiograms of a healthy 18 year old student nurse Relatively large secondary R waves are present in right precordial leads V_1, V V and $_3V_4$ According to some criteria this would be considered as indicative of right ventricular hypertrophy

Initial Right Septal–Late Left Mural Activation
(Left Bundle Branch Block Type)

Complete left bundle branch block is a term which implies that the right ventricle is activated in the usual fashion but that the left ventricular septum and free wall are activated by a delayed and anomalous process Excitation crosses the interseptal junction from the right to the left septal

mass The right septal forces (vector 1, fig 17) representing initial ventricular excitation are not counterbalanced as in the classic normal type of intraventricular activation and therefore can be identified in the clinical electrocardiogram Thus, leads from the right cavity and precordium[4] demonstrate a small, slurred, initial negative deflection, while left cavity and chest leads show a small, reciprocal, initial positive deflection

Little attention has been given to the *right septal deflection* with left bundle branch block In those published reports in which sensitive instruments have been used and the electrocardiographic tracings have been reproduced with sufficient clarity to be evaluated, the small right septal wave can often be identified[1, 8, 18, 4] Also with complete left bundle branch block the electrical forces of the right ventricular free wall (vector 2 of fig 17) are often identifiable in right chest leads as small R waves However, in some cases these are counterbalanced by presumably stronger forces in the septum Delayed and anomalous right to left activation of the left septal mass (vector 3) is responsible for a large negative deflection in the

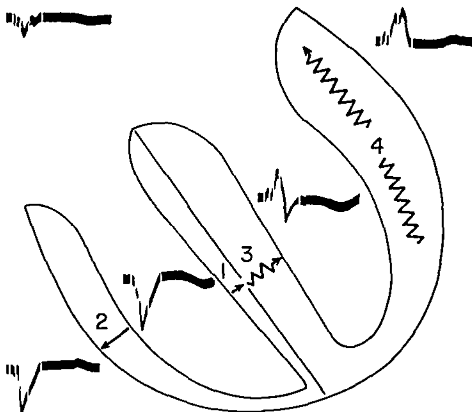


Fig 17 Schema of complete left bundle branch block (initial right septal—late left mural activation) There is reason to believe that the left ventricular cavity lead should be identical with the left precordial lead (see text)

right cavity and in some right chest leads, as well as the second slurred and more prominent upward deflection in left cavity and chest leads.

With left bundle branch block, activation of the left ventricular wall (vector 4) has a strikingly different character than with normal conduction or with right bundle branch block. In unipolar right cavity and chest leads left mural activation produces larger QRS deflections than those with normal conduction. Also, judging from the form of the QRS in multiple precordial leads, the order and duration of left free wall activation is drastically changed. Left mural forces are responsible for the third portion of the upright deflection in left chest leads. In left bundle branch block, as in right bundle branch block, anomalous activation of the free wall on the side of the block may follow a course more parallel, or at least less perpendicular, to the endocardial and epicardial boundaries than normally. If this is true, then leads from within the left ventricular outflow tract should show QRS deflections similar to those from the left precordium.

In our experience, electrocardiograms from the left atrium have demonstrated QRS complexes almost identical with those from left precordial sites in the presence of complete left bundle branch block. Unfortunately leads from within the left cavity were not obtainable.

In many instances of left bundle branch block the right septal forces (vector 1) may not be identified as a distinct deflection in left limb and chest leads. However, more often than not, failure to identify the right septal wave is due to insensitive recording instruments or faulty technique. In some cases the right free wall forces are responsible for a prominent, seemingly initial, negative QRS deflection in left precordial leads. Such a negative deflection may interfere with the diagnosis of left bundle branch block when it is interpreted as a Q wave of left septal origin, or when it raises the question of massive septal infarction. A simultaneous monitor lead from right precordial sites is of aid in identifying the earliest portion of the QRS in left chest leads and in further confirming the presence of a right septal wave (or isoelectric period) and thus of left bundle branch block.

The electrocardiograms reproduced in figure 18 are those of a 50 year old woman with hypertension and longstanding congestive heart failure. Complete left bundle branch block is present. The small initial slurred downstroke of the QRS in lead V_R suggests leftward activation of the septum. A similar deflection is present in leads $_2V_B$, $_2V_4$, V_4, V'_6, $_2V_2$ and V_1. The reciprocal of this deflection is present as a small, slurred upward deflection in left precordial leads (V_4, $_2V_6$, $_2V_B$, V_3, V_5 and V_B).

The right mural forces are represented by a small, slightly later upward deflection in right chest lead (V_6, V_4 and V_1) and a downward deflection in left chest leads ($_2V_6$ and V_5). The latter may easily be misinterpreted as

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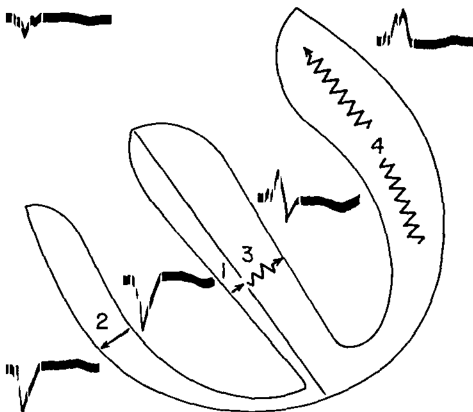


Fig 17 Schema of complete left bundle branch block (initial right septal—late left mural activation) There is reason to believe that the left ventricular cavity lead should be identical with the left precordial lead (see text)

left septal Q waves when the initial right septal influence is not recognized The difficulty in recognizing the right mural deflection in left chest lead is particularly marked when insensitive instruments or careless recording techniques are employed

The anomalous left septal and free wall forces may be merged in the large negative deflection in right precordial leads In left precordial leads the first notch in the R wave suggests a partial separation in the electrocardiographic manifestation of these two forces

The electrocardiograms reproduced in figure 19 illustrate an example of complete left bundle branch block in which the right septal wave would be difficult to recognize without a simultaneous monitor lead The right mural downward deflection in leads I, II V_L V_5 and V_6 superficially resembled a true Q wave when this electrocardiogram was recorded by a less sensitive single channel instrument

Incomplete Left Bundle Branch Block

Recognition of incomplete left bundle branch block presents one of the most difficult problems in electrocardiographic diagnosis This conduction anomaly can simulate as well as obscure the electrocardiographic manifestations of myocardial infarction Also it seems probable that many electrocardiograms at present regarded as characteristic of left ventricular hypertrophy are examples of incomplete left bundle branch block

Wilson pointed out that incomplete left bundle branch block can be excluded when there is a Q wave in one or more leads from the left side of the precordium but that the absence of Q in these leads is of no help Sodi Pallares reasoning from experimental data has suggested certain diagnostic criteria for incomplete left bundle branch block that we believe are not sufficiently precise (see below)

The only difference between the classic normal type of intraventricular activation and minor degrees of low grade incomplete left bundle branch block is in the relative time of onset of excitation in the two ventricles With low grade incomplete left block activation of the left septum is delayed relative to the normal The sequence of spread of excitation within each ventricle is unchanged

Low grade incomplete left bundle branch block of a minor degree is represented by column 2 of figure 20 Such a slight delay in left bundle conduction cannot be recognized in the clinical electrocardiogram The onset of left septal activation is represented as occurring nearly *simultaneously* with that of the right septum

Sodi Pallares has suggested that the most important feature for establishing the diagnosis of incomplete left bundle branch block is initial slurring of the upstroke of the R wave in leads I V_L V_5 and V_6 However,

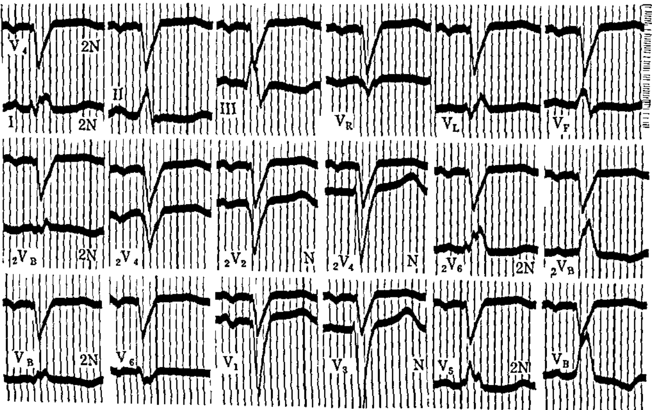


FIG 18 Complete left bundle branch block Note prominent initial right septal waves Female patient age 50 arterial hypertension with congestive heart failure No history suggestive of myocardial infarction

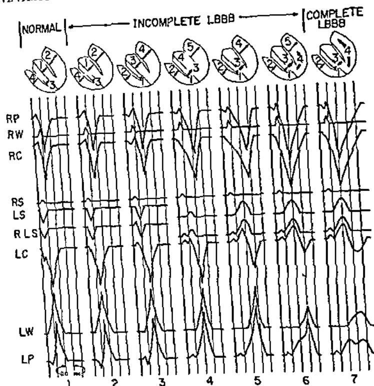


FIG 20 Schema representing progressive gradations of incomplete left bundle branch block between classical normal intraventricular conduction and complete left bundle branch block

there are reasons to question the reliability of this sign Such slurring is present in 50 per cent of the electrocardiograms of healthy young subjects in which there is no suggestion of incomplete left block (See figs 11 and 12)[14] On the other hand electrocardiograms clearly indicative of initial ventricular activation beginning in the right septum and thus compatible with this concept of incomplete left block may show no suggestion of initial R wave slurring in leads V_5 to V_7 (fig 21)

Sodi Pallares[27] has also emphasized the absence of Q waves in leads I V_L V_5 and V_6 as a diagnostic criterion of incomplete left bundle branch block However it is not uncommon for Q waves to be absent in leads V_5 and V_6 when left bundle branch block is not present This is often due to the particular relation of these chest sites to the heart rather than to a delay in conduction (fig 11) In leads further to the left (i e V_7 and V_8) normal Q waves may be encountered On the other hand an early negative QRS deflection resembling a Q wave and not representing initial left septal but rather right mural or delayed left septal activation may be

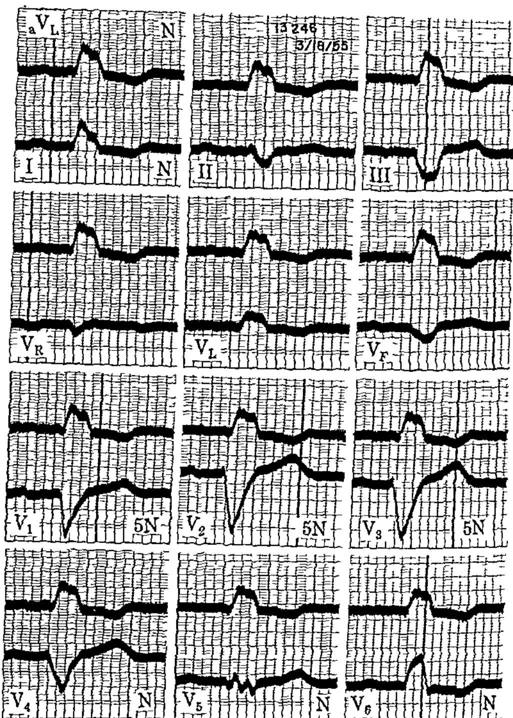


FIG 19 Complete left bundle branch block Note right septal waves Male patient age 75 normal blood pressure and no history of myocardial infarction

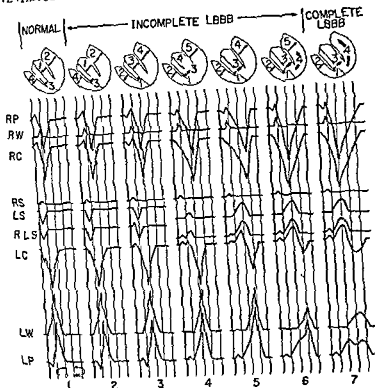


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Sodi Pallares[42] has also emphasized the absence of Q waves in leads I V_L V_5 and V_6 as a *diagnostic* criterion of incomplete left bundle branch block However it is not *uncommon* for Q waves to be absent in leads V_5 and V_6 when left bundle branch block is not present This is often due to the particular relation of *these* chest sites to the heart rather than to a delay in conduction (fig 11) *In leads* further to the left (i e V_7 and V_8) no ... Q waves may be encountered On the other hand an early negative QRS deflection resembling a *Q wave* and not representing initial left septal but rather right mural or *delayed left* septal activation may be

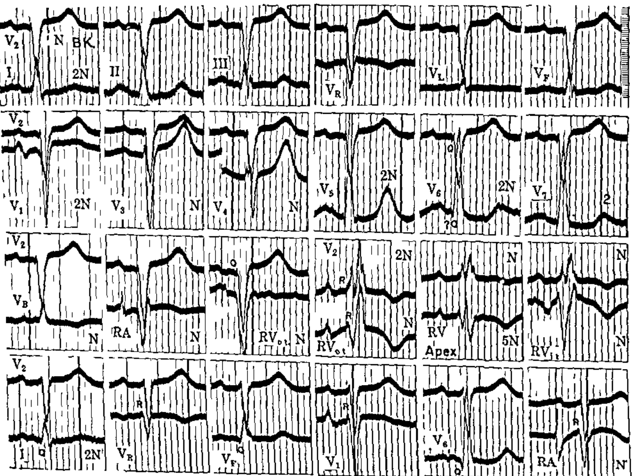


Fig 21 Low grade incomplete left bundle branch block transient complete right bundle branch block during right ventricular catheterization followed by low grade incomplete right bundle branch block Pseudo Q waves (S waves) are present in leads V_5 V_6 and V_7 with incomplete left block Q waves in leads V_R V_2, and right cavity leads disappear with right block R waves in V_4 are identical in incomplete right and left bundle branch block

present in leads I, V_5, V_6 with left bundle branch block as already noted (fig 19 21 22 and 23)

It would seem reasonable to restrict the clinical diagnosis of incomplete left bundle branch block only to those cases in which there is clear electrocardiographic evidence of initial ventricular activation beginning in the right septum [43]

A greater degree of incomplete left bundle branch block is represented in column 3 of figure 20 The right septal forces (vector 1) are indicated by the positive deflection of the right septal (RS) electrogram as beginning *before* those of the left septum (vector 3) The forces of the left septum are represented by a negative deflection in the left septal (LS) electrogram as commencing shortly *after* the onset and continuing after right septal activation Therefore right septal excitation precedes that of the left septum and is responsible for a small initial, negative deflection in right cavity (RC) and precordial (RP) leads and a small initial positive deflection in left cavity (LC) and precordial (LP) leads

In clinical electrocardiograms the initial right septal forces are often represented by an indistinct positive deflection or an isoelectric phase in unipolar left chest lead Their recognition often requires special instrumentation and recording techniques as has been discussed in reference to complete left bundle branch block

When activation of the right ventricular free wall (vector 2) represented by a positive deflection in the right mural electrogram (RW) occurs more or less at the same time as the *delayed* rightward activation of the left septum (vector 3) represented by the negative deflection of the left septal electrogram (LS of column 3 fig 20) summation of these two sets of forces may occur before the rapid development of strong left mural forces Left septal and right mural forces may be responsible for a prominent slightly delayed R wave in right *chest lead* (*RP*) and an early negative deflection in left chest leads (i e S wave)

When the right septal R wave in left chest leads is indistinct the relatively early negative deflection due to summated left septal and right mural forces may be mistakenly identified in a physiologic sense as a Q wave (figs 19 21 22 and 23)

Activation of the left ventricular free wall (vector 4) in the theoretical grade of *incomplete left bundle branch block* represented in column 3 of figure 20 is the same as that with the classic normal type of intraventricular conduction and incomplete right bundle branch block (fig 21)

The electrocardiograms reproduced in figure 21 are those of a 75 year old female with arterial hypertension mitral stenosis and chronic congestive heart failure The pulmonary *artery* pressure was 87 37 and the right ventricular pressure 87 5 mm Hg The electrocardiograms in the upper

two rows and the first three complexes of the third row represent low grade incomplete left bundle branch block, similar to that of column 3 figure 20. The QRS interval is 0 10 sec. The initial portion of the QRS complex in the unipolar right arm lead, right precordial leads (V_1, V), and intracavity right atrial and ventricular leads resemble those with complete left bundle branch block.[24] The Q wave in the monitor lead V_2 indicates that the early negative deflection in leads V_5 to V_7 does not represent initial ventricular activation, as superficial inspection of a single channel recording would suggest. However, critical examination of these left precordial leads reveals the presence of a small initial R wave occurring synchronously with the Q wave of lead V_2. Therefore the early negative deflection in the left precordial leads is an S wave. The unipolar posterior left chest lead V_8 shows a nearly isoelectric phase during the interval of right and left septal activation. The right ventricular cavity lead shows a small upward notch on the descending limb of QS that is probably due to delayed rightward activation of the left septum.

During the course of right ventricular catheterization incomplete left bundle branch block was temporarily replaced by complete right bundle branch block with prolongation of the QRS interval to 0 14 sec. The last three complexes of the third row of figure 21 are electrocardiograms from three different, right ventricular cavity sites while complete right bundle branch block was present. The QS wave in right cavity and chest leads and the Q wave in right chest leads were replaced by an initial, positive deflection of left septal origin followed by relatively early secondary, positive deflections suggesting anomalous right septal activation, and, finally, by large, late, positive deflections representing anomalous activation of the right ventricular free wall. The differences in form of the initial QRS complex of electrocardiograms from various right cavity sites are largely duplicated in leads from various right precordial sites when complete right bundle branch block is present. Also the pseudo Q wave (i e S wave) in left chest leads was replaced by true Q waves (not shown in fig 21).

When the tip of the catheter was withdrawn from the ventricle to the atrium, complete right bundle branch block was replaced by low grade incomplete right block with a QRS interval of 0 10 sec. This is demonstrated in the electrocardiograms in the fourth row of fig 21. The initial R wave in leads V_R, V_1, V_2 and the unipolar right atrial lead (RA) and the Q wave in leads V_F and V_6 suggest that initial ventricular activation commenced in the left septum. The late upward notch or slur in the QRS complex of lead V_R suggests delayed activation of the right ventricular free wall.

The almost identical appearance of the deflections occupying the first 0 09 sec of the QRS complex in lead V_6 with incomplete right and left

bundle branch block indicates that the sequence of activation within the left ventricular free wall is essentially the same in both in this particular instance

The electrocardiograms reproduced in figure 22 are those of a healthy 30 year old man and are similar in some pertinent aspects to those of figure 21 The initially slurred Q wave in lead V_R the Q waves in high esophageal leads (E_{24} and E) the small Q waves in high right chest leads V_1, $_2V$, and $_3V_3$, and the right chest lead V_4 and the initial R waves in lower esophageal leads E_{44} and E_{50} and left chest leads V_6 and V_7 are strongly indicative of initial right to left activation of the right septum

The early negative deflection in leads I V_L V_B and $_2V_6$ occurs later than the Q wave in high right precordial leads Figure 23 shows leads $_2V$ and V_6 of figure 22 recorded simultaneously The difference in time between the onset of the Q wave in $_3V_2$ and the early negative deflection in V_6 is approximately 0 005 sec This finding is further substantiation of initial ventricular depolarization beginning in the right septum and therefore suggests either a delay in left bundle branch conduction or a relatively *more rapid* conduction in the right bundle branch

The notch in the final portion of the QRS complex of lead V_R does not represent the embryonic R wave which ordinarily suggests final rightward activation of the right ventricular or septal base It is due *rather to some force of unknown cardiac origin pointing to the left The upright* reciprocal of the late QRS *notch in* V_R is prominently displayed in leads I II V_F V_5 V_6 V_7 V_B and the lower esophageal leads (E_{44} and E_{50}) as a slurred P of 0 03 sec duration This deflection is commonly present in electrocardiograms of young healthy subjects[14] *as well as in those* of patients with heart disease (Fig 4) [25] *The animal studies* of Scher [17] demonstrating final ventricular activation in the base of the interventricular septum suggest this origin *for this wave*

The shortest QRS intervals in healthy subjects are found with minor degrees of incomplete left bundle *branch* block (initial right septal-late left mural activation)

It was pointed out previously that *secondary* R waves long present in youth in high right chest lead may appear later in life in leads V_1 and V_2 as the result of a lowering of the heart secondary to pulmonary emphysema or some other factor altering the heart's position A similar change in the heart's position may account for the appearance of right septal Q waves of incomplete left bundle branch block *in conventional* right precordial leads of older subjects with pulmonary emphysema

In accord with the concept that left bundle branch conduction is shorter than right branch *conduction the average* P R interval of healthy young subjects with electrocardiograms suggesting *initial* left septal activation

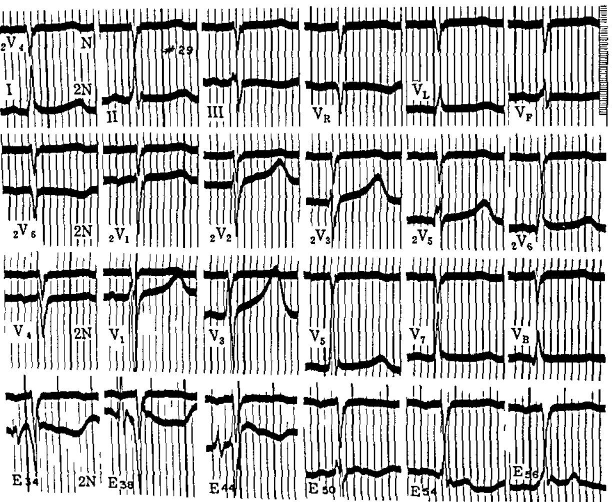


Fig 22 Low grade incomplete left bundle branch block Healthy 30 year old male subject Note terminal slurring of QRS complex

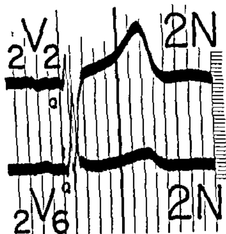


FIG 23 Simultaneous lead $_2V_2$ and $_2V_6$ from same subject as in figure 22 The Q wave in lead $_2V_2$ occurs 0 005 sec before the initial negative QRS deflection in lead $_2V_6$

was 0 164 sec and with initial right septal activation was 0 176 sec [14] However there is a great overlapping of individual values The range of the P R interval in the former group was 0 11 to 0 20 sec and in the latter group was 0 13 to 0 23 sec An absolute measurement of the P R interval is of no aid in determining the type of intraventricular conduction in a specific subject

These data correlating the P R interval with types of intraventricular conduction are based upon findings in only 100 patients and therefore may be fortuitous If such is the case low grade incomplete left bundle branch block may not be representative of delayed left bundle branch conduction Early excitation of the right septum by an unrecognized A V conduction mechanism is perhaps as logical an explanation as is a delay in left branch conduction

Electrocardiograms similar to those of figures 21 and 22 characteristic of incomplete left bundle branch block have been ascribed by some investigators to right ventricular hypertrophy [3 44 45] left septal fibrosis [47] anteroseptal myocardial infarction [48] high anterior myocardial infarction [49 50] and peri infarction block [51 5] Although there is no question but that each of these conditions may be concommitantly present with incomplete left bundle branch block, the latter should not be regarded as necessarily suggestive of the former Actually low grade incomplete left bundle branch block also occurs in healthy young subjects [14]

High-grade incomplete left bundle-branch block with sufficient delay in left branch conduction to permit partial anomalous left septal activation

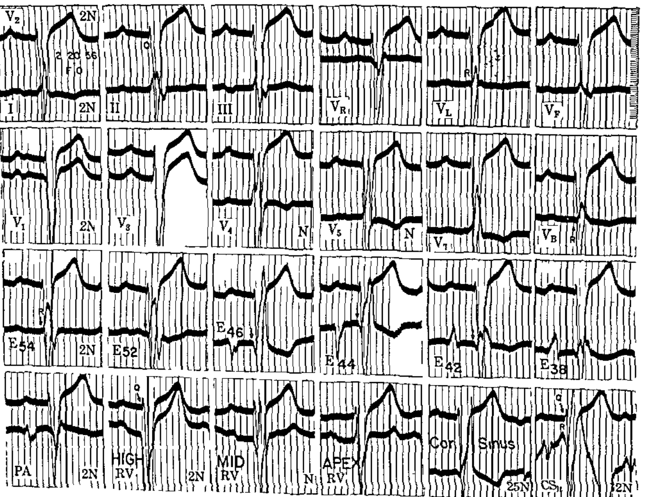


FIG 24 High grade incomplete left bundle branch block Male patient age 68 advanced pulmonary emphysema and fibrosis with chronic congestive heart failure

from the right is illustrated in column 4 of figure 20 Activation of the free left ventricular wall occurs in the normal fashion The great difference in the time of onset between right and left septal activation allows the right septal force to become prominent as with complete left bundle-branch block Partial anomalous activation of the left septum is indicated by an extension of the right septal process (vector 1) across the interseptal junction into the left septum (vector 3) The left septal electrogram (LS) becomes upright and slurred Thus the initial excitation of the left septum by the anomalous process produces a prominent slurred upward deflection in the left cavity (LC) and chest leads (LP) The slurred initial portion of the QRS complex is similar in character to that of anomalous atrioventricular excitation (Wolff Parkinson White syndrome) [33] The forces of the left ventricular free wall are the same as those with normal conduction However rather than being opposed by the forces of the right ventricular wall and left septum they are augmented by the partial anomalous left septal excitation Therefore the negative deflections in the right cavity (RC) and precordial (RP) leads and the positive deflections in the left chest leads are larger than those with normal conduction (fig 26)

The electrocardiograms reproduced in figure 24 are those of a 68 year old man with arteriosclerotic heart disease pulmonary fibrosis and emphysema and long standing chronic congestive heart failure The pulmonary artery pressure was 85 37 and the right ventricular pressure 80 22 mm Hg High grade incomplete left bundle branch block similar to that represented by column 4 figure 20 is present

Complete anomalous activation of the left septum with normal conduction in the left ventricular free wall is illustrated in column 5 of figure 20

A theoretically still greater degree of high grade, incomplete block on the left in which all of the left septum and part of the left ventricular free wall is anomalously activated cannot be distinguished clinically from complete left bundle branch block (fig 20 column 6) Rapid final excitation of the left ventricular free wall by the normal process delivered from the left bundle branch is responsible for a prominent late deflection similar to that seen with high grade anomalous atrioventricular excitation [33]

Incomplete Left Bundle Branch Block and Left Ventricular Hypertrophy

In the presence of long standing arterial hypertension or other conditions imposing a great work load on the left ventricle it is generally recognized that the left ventricular septum as well as the free wall may be greatly hypertrophied Electrocardiograms with unusually large S waves in right chest lead and large R waves in left chest leads are regarded as due to an abnormally large voltage generated by the hypertrophied free wall [1 8] However the R wave in right chest leads and the Q wave in left chest

leads both representing the forces of the left septal mass frequently are not proportionally increased in amplitude, as would be expected with hypertrophy of the left septum[1] In fact, right precordial R waves and left precordial Q waves are often absent or unusually small[1]

Rasmussen[54] has suggested that the electrocardiographic findings in many patients with left ventricular hypertrophy are due to defects in left bundle branch conduction Inspection of electrocardiograms reproduced in many classic reports and presented as typical of left ventricular hypertrophy reveals many with QRS configurations characteristic of high grade incomplete left bundle block[1, 8, 55]

The large QRS deflections seen with left ventricular hypertrophy are often dramatically reduced in size as the result of the oral administration of potassium salts[56] dietary sodium restriction[57] and sympathectomy[58] This change in size is not always correlated with lowering of blood pressure decrease in heart size or improvement of congestive heart failure Several explanations have been suggested, but the mechanism for the reduction in QRS amplitude following these procedures is not known These data suggest that factors in addition to hypertrophy may be responsible for the large amplitude of the QRS complex Confusing however is the fact that potassium salts, sodium restriction and sympathectomy do not alter the order of intraventricular conduction in the presence of incomplete left bundle branch block

In a study of 74 patients with arterial hypertension Bryant and Murtadha[59] found that only 10 per cent demonstrated electrocardiograms with abnormally large QRS deflections suggestive of left ventricular hypertrophy in accordance with the criteria of the New York Heart Association[60] By these criteria for high voltage of QRS a deflection on one side of the reference level must exceed 2 0 mv in any of the augmented unipolar extremity leads or 5 0 mv in any of the usually recorded six precordial leads Thirty per cent of this group showed electrocardiographic configurations consistent with incomplete left bundle branch block as described above In young healthy subjects[14] the incidence is only 13 per cent Thirty two per cent of the hypertensive patients had normal electrocardiograms[59]

Figure 25 shows the electrocardiograms of a 70 year old man with arterial hypertension of long standing The over all picture is typical of so called "left ventricular strain However the monitor right chest lead V_1 contains a prominent Q wave which is definitely earlier than the negative deflection of left chest lead V_6 This finding confirms the presence of incomplete left bundle branch block

Just as transient right bundle branch block can suddenly change the form of the normal electrocardiogram to the pattern regarded by some as

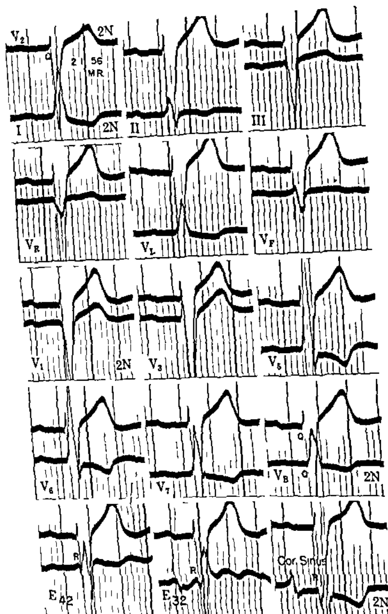


FIG 25 Left ventricular train pattern with low grade incomplete left bundle branch block Male patient age 0 long standing arterial hypertension

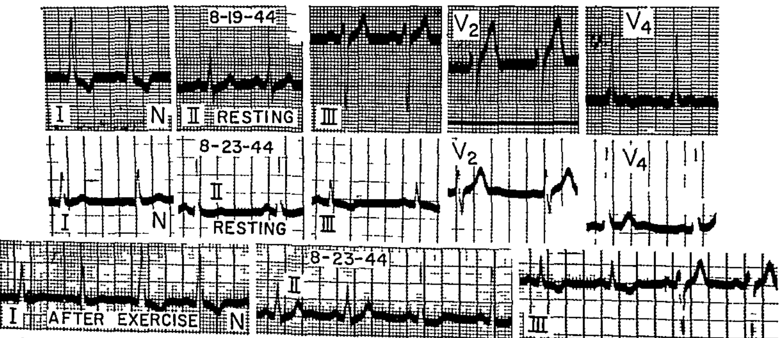


Fig 26 Transient high grade incomplete left bundle branch block resembling so called left ventricular "strain" pattern Incomplete left bundle branch block appears with increased sinus rate Healthy subject without symptoms or signs of heart disease (From Wilson et al Advances in Internal Medicine fig 13 [1])

typical of right ventricular hypertrophy[19] so can transient, incomplete left bundle branch block duplicate the pattern of so-called *left ventricular strain* The electrocardiograms of figure 26 from an article by Wilson[3] illustrate high grade incomplete left bundle-branch block when the rate is 88 per min (upper row) and normal conduction with a slower rate (middle row) *Transition from normal conduction to left block*, as a result of increase in the heart rate, is demonstrated in the third row Thus recognition of incomplete left bundle branch block as a possible cause of, or contributing factor to the electrocardiographic pattern of left ventricular hypertrophy is of practical importance

The Vectorcardiogram and Incomplete Left Bundle Branch Block

Three dimensional vectorcardiograms using the Wilson tetrahedron[61] and high amplification where recorded from 14 subjects with *clear-cut electrocardiographic* evidence of incomplete left bundle branch block as defined[62] *In only* 7 subjects was there vectorcardiographic evidence of initial right to-left activation of the interventricular septum* The *failure of the vector*cardiogram to demonstrate initial right sided septal activation *is probably due to the relatively great distance of the electrodes from the heart in the* reference frame used[63]

Initial Right Septal—Late Right Mural Activation
(Bilateral Incomplete Bundle Branch Block Type)

We have referred to initial right septal—late right mural activation in previous papers[14, 15] as bilateral incomplete bundle branch block because with this type of conduction *the initial* QRS deflections are characteristic of left bundle branch block *and the latter* portions resemble those in right bundle branch block[23]*

The electrocardiograms *reproduced in figures 27 and 28 are* those of a 70 year old man with long standing arterial hypertension (*180/100 mm Hg*) and chronic congestive heart failure The QRS interval is 0 114 sec Figure 29 is a drawing *representing these electrocardiograms* as if they were recorded simultaneously in order *to illustrate* their time relationships Lead V serves as a constant reference *point for* each lead Measurements were made after magnifications *of 18×* (equivalent to 54× with a paper speed of 25 mm per sec) and are accurate to 0 001 sec The right *cavitary* unipolar leads suggest that initial right *to-left activation* commences in

* Sodi Pallares[9] disagrees with this concept of bilateral incomplete bundle branch block His opinion is based on the *experience of* not having been able to produce a block of the right bundle *peripheral* to the septum by numerous endocardial cuts on the right ventricular wall He believes that delayed activation of the free wall of the right ventricle cannot *occur when* the right septum is activated normally Clinical intracavitary electrocardiographic observations suggest the contrary

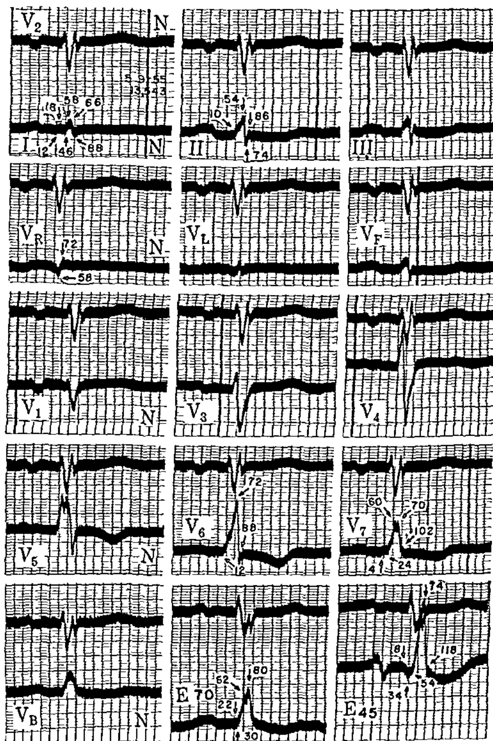


FIG 27 Bilateral incomplete bundle branch block Electrocardiogram fulfills criteria for both incomplete right and left bundle branch block Male patient age 70 arterial hypertension and chronic congestive heart failure

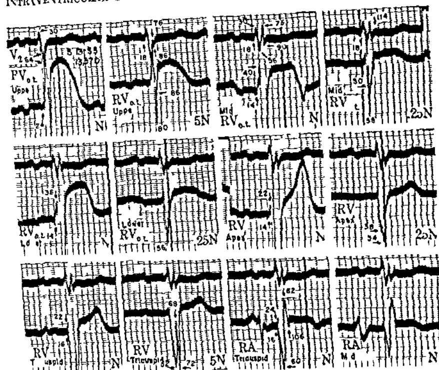


FIG 28 Right intracardiac leads from the same subject represented in figure 27 Note disappearance of Q waves in leads from lower outflow tract apical and outflow tract sites when standardization is reduced to such a degree that all of the QRS complex is recorded on the graph

the superior portion of the right septum and is followed 0 014 sec later by excitation of the left mid septum in the opposite direction accounting for the slightly delayed first R wave in lead V_2 The latest positive QRS peak in the right cavitary lead occurs 0 012 sec before a similar deflection in the unipolar right precordial lead This suggests that right ventricular muscle between the right cavity and precordium is responsible at least in part for the final portion of the secondary R wave in lead V_2

A similar type of intraventricular conduction with a greater degree of delay in activation of both the left septum and the right ventricular free wall is represented in the electrocardiograms reproduced in figure 30 The prolongation of the QRS interval to 0 16 sec and the slurred late R wave in lead V_1 suggest that the right ventricular free wall is activated entirely by an anomalous process similar to that with complete right bundle branch block Necropsy revealed right ventricular hypertrophy of an advanced degree

Figure 31 shows the electrocardiograms of a 28 year old healthy phy i

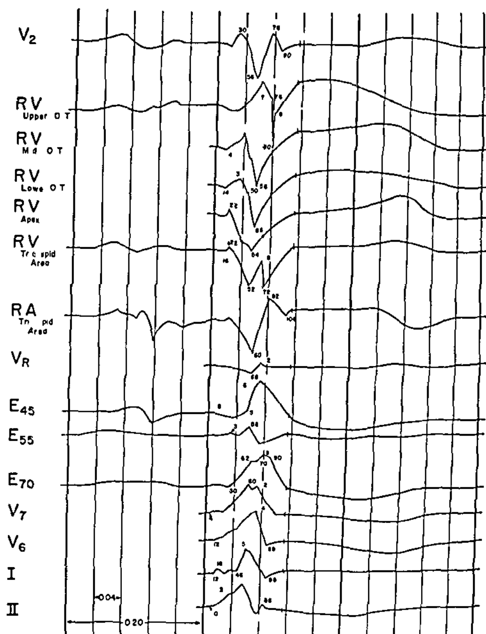


Fig 29 Simultaneous representation of leads reproduced in figures 27 and 28

cian The QRS interval is 0 14 sec The slurred Q wave in V_R small slurred Q waves in right chest leads ${}_2V_1$ ${}_2V_2$ V_3 and absent Q waves in left chest leads V_6 and V_7 are compatible with initial leftward excitation of the right septum The Q waves in leads V_R ${}_2V_2$ and V_3 occur earlier than the early negative deflection in V_6 and V_7 The late secondary R waves

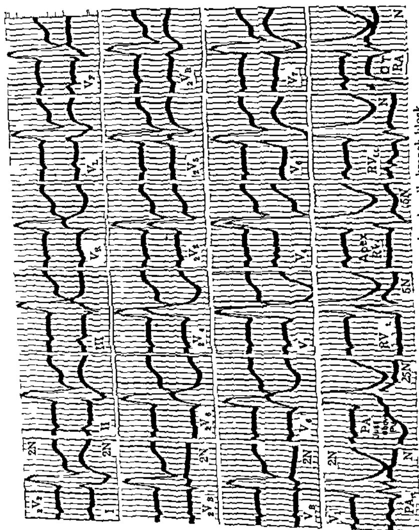


Fig 39 High grade bilateral incomplete bundle branch block

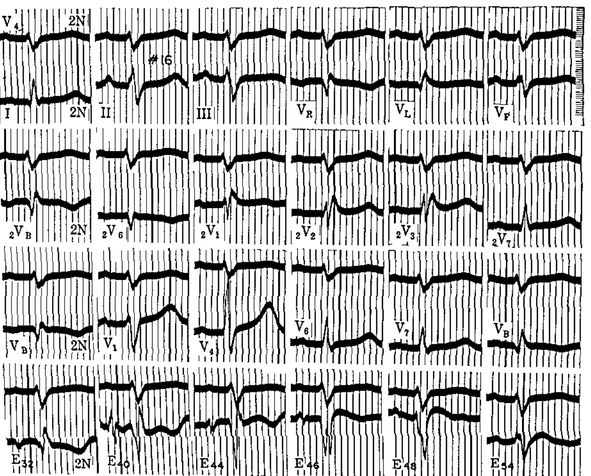


Fig 31 Bilateral incomplete bundle branch block Healthy 28 year old physician

in leads V_6 through $_2V_3$ and lead V_R suggest delayed activation of the free wall of the right ventricle These findings are therefore compatible in the electrocardiographic sense with a concept of delayed activation of both the left septum and the free wall of the right ventricle

The QS deflection in lead E_{16} is of interest in view of the fact that similar findings have been considered as characteristic of posterior myocardial infarction However there was no indication that this 28 year old physician had any cardiac disease

LEFT BUNDLE BRANCH BLOCK AND MYOCARDIAL INFARCTION

The difficulty inherent in electrocardiographic diagnosis of myocardial infarction in the presence of complete left bundle branch block is well recognized[1] It is only during the acute phase when RS T segment displacement is present that the electrocardiogram provides strong suggestive evidence of myocardial infarction

Minor degrees of low grade incomplete left bundle branch block (fig 20 column 2) do not interfere with the development of QRS changes characteristic of myocardial infarction With slightly greater degrees of low grade (column 3 fig 20) and minor degrees of high grade incomplete left bundle branch block (column 4 fig 20) myocardial infarction can cause conspicuous early S waves (i e Q wave equivalents) in left lateral chest leads Such S waves due to anterolateral myocardial infarction in the presence of high grade incomplete left bundle branch block (column 4 fig 20) are present in leads V_5 $_2V_5$ and V_6 of figure 32 and are due to the forces from the delayed partial left to-right activation of the left septum

Incomplete left bundle branch block of the degree indicated in columns 3 through 5 of figure 20 because of the right septal deflections (Q waves) in leads $_3V_1$ through $_2V_2$ V_1 V_2 and sometimes V_3 may simulate the QRS configurations of anteroseptal myocardial infarction (see figs 18 21 22 24 25 and 27 31)

Massive transeptal infarction with complete left bundle branch block is indicated in the electrocardiograms of figure 33 Initial ventricular activation occurs in the free wall of the right ventricle Thus R waves in lead V_R and right precordial leads and Q waves in left precordial leads are due to the forces originating in the free wall of the right ventricle

PARIETAL VENTRICULAR BLOCK

Alzamora Castro[65] has shown that focal ventricular blocks produced experimentally can cause electrocardiographic abnormalities indistinguishable from those seen with various degrees of bundle branch block When focal block involves small areas of myocardium the characteristic electrical effects can only be recorded in direct leads from the involved

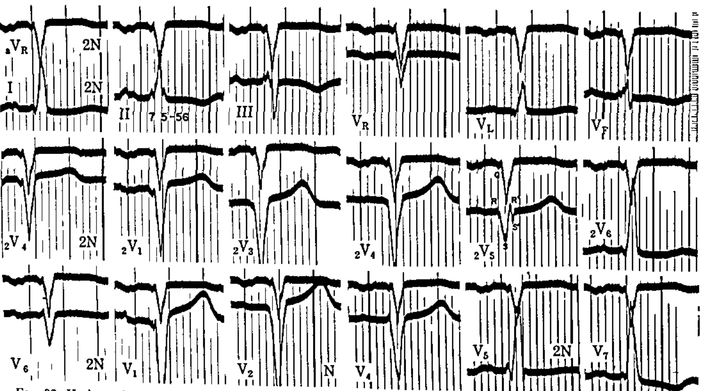


Fig 32 High grade incomplete left bundle branch block with extensive old anterior myocardial infarction Male patient age 61

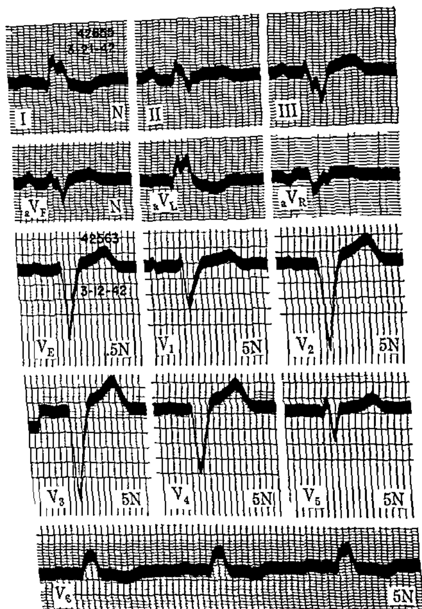


FIG 33 Complete left bundle branch block with massive septal myocardial infarction (From Pantridge Circulation [72])

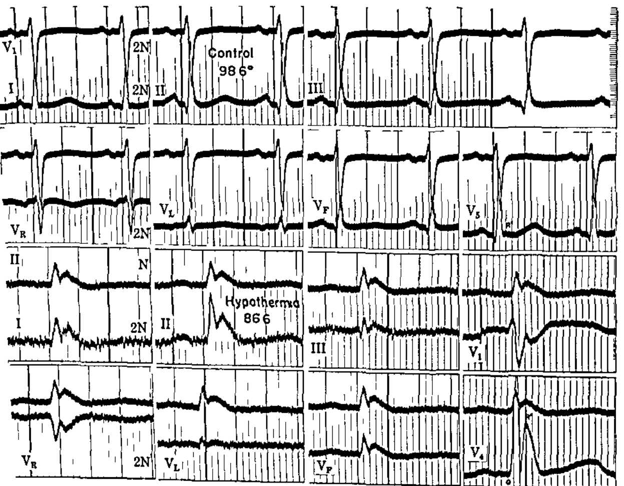


Fig 34 Electrocardiograms before and during hypothermia Parietal ventricular block Note large secondary upward deflections during hypothermia suggesting most marked parietal block in basal septal area with right to left activation

site When the focal block is pronounced intracavitary leads show the same QRS configurations as epicardial leads from the involved ventricle This relationship is similar to that found with complete right bundle branch block which is illustrated in figure 5

All types and degrees of parietal ventricular block may be superimposed upon other kinds of intraventricular anomalies secondary to variations in the specialized conduction system An example of parietal ventricular block is shown in figure 34 The subject was a healthy 30 year old woman The two upper rows of tracings are characteristic of the classic normal type of intraventricular conduction as previously defined A prominent slurring of the terminal portion of the QRS complex is seen in lead V_1 that is simultaneous with a small slurred upward deflection in lead V_6 Scher[17] has published electrocardiograms obtained from sites high in the posterior interventricular septum demonstrating a small deflection occupying the same portion of the QRS complex This deflection was thought to be due to late activation of some muscle in the basal region of the interventricular septum *

The third and fourth rows of electrocardiograms of figure 34 were recorded during induced hypothermia At a body temperature of 86 6 F the sinus rate fell from 100 to 38 per min the P R interval increased from 0 14 to 0 22 sec and the QRS interval lengthened from 0 09 to 0 28 sec The initial 0 06 sec phase of the QRS complex increased to about 0 09 sec during hypothermia indicating prolongation of activation in the main ventricular muscle mass compatible with a considerable degree of parietal block The most striking changes during hypothermia occurred in the small slurred terminal deflection of the QRS complex and is most dramatically illustrated in lead V_4 The amplitude of this deflection increased 300 per cent and its duration from 0 03 to 0 12 sec These findings suggest that the greatest parietal block was present in the basal region of the interventricular septum Similar changes were observed in the electrocardiograms of thirty dogs submitted to hypothermia [67]

At present there is no satisfactory means of recognizing parietal ventricular block in the clinical electrocardiogram except under specific circumstances when drugs with quinidine like effects have been used Changes suggesting its occurrence are frequently observed just prior to death

Recognition of the unusually slow terminal activation process in the base of the interventricular septum[17] suggests that a degree of parietal ventricular or muscle fiber block may be physiologic This also raises the question as to whether or not the U wave is the wave of repolarization (i e T wave) of the base of the interventricular septum

* Kossmann[4] believes that this deflection is due to ventricular repolarization

Comparison of Intraventricular Conduction in Healthy Subjects and in Patients with Heart Disease

Table I is an analysis of the types of intraventricular conduction suggested by the electrocardiograms of 100 healthy young subjects below 40 years of age[14] and 100 selected (for technical reasons) patients over 40 years of age with, or suspected of having heart disease[26] Each group was made up of 50 males and 50 females

The older subjects represent a group of patients who had consecutive, routine electrocardiographic examinations However, those with atrial fibrillation, myocardial infarction and artifacts which would interfere with identification of the QRS deflections were excluded

The terminology for the types of intraventricular conduction is that used in the preceding discussions and does not include peculiarities in the S T segment and T waves

The QRS interval was measured in each extremity and chest lead of each subject The longest interval was considered as the most accurate representation of the intraventricular conduction time In the majority of records the longest interval was found in a unipolar chest lead as illustrated in figure 7 Therefore, these measurements are not comparable to conventional values obtained from the Einthoven limb leads

The range of values for the QRS interval indicates the limitations of these measurements as an adjunct in identifying the different types and degrees of intraventricular conduction They also indicate that intraventricular conduction is frequently shorter in patients with heart disease than in healthy young subjects This peculiarity is most marked in patients with atrial fibrillation[38] Thus it is apparent that the QRS interval *per se* is of little or no value in determining the pathologic significance of electrocardiographic peculiarities

Table I *Classification of Intraventricular Conduction in 100 Healthy Subjects and 100 Cardiac Patients*

	Types of Intraventricular Conduction			Healthy Subjects			Cardiac Patients*		
	Conventional Nomenclature	Sequential Classification of Intraventricular Conduction		No	QRS Interval		No	QRS Interval	
					Range	Mean		Range	Mean
1	Classical Normal	Initial left septal late left mural	RS	2	10- 1	11	50	08- 1	10
2	Right BBB	Initial left septal late right mural	RSR	85	09 13	11	19	09 16	10
3	Left BBB	Initial right septal late left mural	QS	3	09 10	10	9	08- 1	11
4	Bilateral Incomplete BBB	Initial right septal late right mural	QRSR	10	10- 14	10	3	09 21	13

* Based on the form of the QRS complex in right-sided leads

The finding of the classic normal type of conduction (initial left septal-late left mural activation) in only 2 per cent of healthy young subjects and in 50 per cent of the older cardiac patients is of particular importance when considered in relation to the occurrence of initial left septal-late right mural activation (right bundle branch block type) Blount[18] has reported secondary R waves in right chest leads compatible with this concept of delayed right ventricular wall activation in 98 per cent of a series of 50 healthy children (age range not stated) Secondary R waves in right chest leads were present in 95 per cent of the 100 healthy subjects in this series below 40 years of age[14] whereas only 22 per cent of patients above 40 years of age demonstrated similar findings[26]

This surprising discrepancy between the occurrence of the classic normal and initial left septal-late right mural activation (right bundle branch block type) suggests some unusual implications First the right bundle branch block type of conduction may represent a fetal remnant' and the predominant order of intraventricular conduction in young healthy adults On the other hand the classic normal type may represent an evolution to a more mature state or may be the result of a pathologic process Second, the numerous reports (refs 68 69 and others) emphasizing the value of the electrocardiogram as an aid in the diagnosis of interatrial septal defects when so called incomplete right bundle branch block is present may represent the inherent error of investigators finding what they are looking for' in view of the fact that secondary R waves some of which are relatively large in right chest leads of healthy children and young adults is the predominant normal (Chapter 13)

SUGGESTED NOMENCLATURE FOR TYPES OF INTRAVENTRICULAR CONDUCTION

In view of the strong pathologic connotation of the term bundle branch block a different and simpler nomenclature would seem to be indicated Such a change in nomenclature could facilitate a break with the concept that electrocardiographic abnormalities in themselves are disease

Each of the four types of intraventricular conduction has a characteristic QRS configuration that is most reliably recognized in right sided leads Most frequently it is found in the unipolar right arm lead There fore it seems reasonable that right precordial leads and leads V_R or aV_R could serve as a convenient basis for a purely descriptive electrocardiographic classification[70] in conjunction with the established nomenclature of the American Heart Association[87]

The classic type of normal intraventricular conduction with initial left septal and late left mural activation characteristically shows small R waves and large S waves in the unipolar right arm and right precordial

leads Thus, the term "RS type" is a simple and accurate designation (Table I) For this purpose, capital letters are adequate

Recent publications[11, 16] have referred to initial left septal-late right mural activation as the "RSR type" of conduction because of the rSr′ deflections in right chest leads The term "RSR type" is conventionally and descriptively appropriate to designate this sequence of intraventricular activation in which the QRS deflections resemble or are indicative of right bundle branch block

With initial right septal and late left mural activation, a QS or qrS deflection is present in leads V_R, aV_R and right chest leads The term "QS type" is convenient to indicate simply and accurately this kind of intraventricular conduction in which electrocardiographic characteristics of *left bundle branch block are present*

The initial right septal and late right mural activation type of conduction is characteristically accompanied by qrSr, qrSrs or Qr in right sided leads The term "QRSR type" is descriptively appropriate for this type of intraventricular activation having electrocardiograms characteristic of bilateral, incomplete bundle branch block

Each of these terms for the four basic types of intraventricular conduction can be supplemented by designations of other strictly electrocardiographic characteristics The duration of the QRS interval can be stated *per se* thus eliminating the difficulty of attempting to distinguish between 'incomplete' and complete bundle branch block or between electrocardiograms with similar configurations

From past experience it is evident that whatever new nomenclature, if any, may ultimately evolve a dogmatic terminology with stereotyped clinical implications is undesirable The practical difficulty of discarding electrocardiographic terms once they have been widely accepted as having specific *clinical significance, has been demonstrated frequently in the past* A simple descriptive classification emphasizing the *sequence* of rather than delay in ventricular activation has obvious advantages over previous classifications It emphasizes the similarity of intraventricular conduction in health and disease and it should aid in calling the attention of the student to the limited clinical specificity of most electrocardiographic diagnoses

Summary

Problems concerning the identification and the clinical significance of common types of intraventricular conduction have been discussed and defined within the limits of present knowledge

The most significant aspect of this material is the demonstration that the majority of so called defects in intraventricular conduction are sug

gested in the electrocardiograms of healthy young subjects. Some of these electrocardiographic peculiarities closely resemble or are identical with those conventionally regarded as indicating serious heart disease. It is therefore appropriate to re-emphasize Wilson's admonition that "electrocardiographic abnormalities are not diseases."

Values of the QRS interval have been demonstrated to be unreliable in differentiating between so-called incomplete and complete bundle branch block.

Secondary R waves in leads from the right side of the body occur in the majority of healthy young people (95 per cent). These fulfill previous criteria for right bundle branch block. This finding is interpreted to indicate that a delay of excitation to the free wall of the right ventricle is the predominant normal. It is suggested that secondary R waves in right chest leads may be a fetal remnant because of their infrequent appearance in the electrocardiograms of older subjects with or suspected of having heart disease.

Electrocardiographic findings characteristic of the classical concept of normal intraventricular conduction are recorded infrequently in healthy young subjects but frequently in older patients. Whether this type of intraventricular conduction indicates a mature state or is the result of an aging or pathologic process is problematical.

The high correlation between secondary R waves in lead V_R and unipolar right chest leads indicates that the unipolar right arm lead is highly reliable in detecting delayed activation of the right ventricular free wall. However there is no reliable means of determining whether secondary R waves in right chest leads are indicative of health or disease unless they have been recognized as having developed in serial tracings *unrelated to changes in position of the heart or of the chest electrodes* and unless they can be correlated with other clinical and laboratory data indicating a pathologic process.

The possibility of falsely interpreting the upstroke of S waves in right sided leads as late R waves of right wall origin when terminal leftward directed septal forces are present is stressed. It is suggested that the terminal septal wave indicating right to left activation at the septal base represents a physiologic type of parietal or focal ventricular block. Repolarization of this area may be responsible for the U wave (i.e. the T wave of the interventricular septal base).

A technique that facilitates identification of characteristics of incomplete left bundle branch block (i.e. initial right septal activation) is described. Simultaneously recorded leads from the right arm and left chest sites provide a more precise means for recognizing initial septal excitation than do conventional techniques. The augmented unipolar right arm lead of Goldberger (V_R) recorded at twice normal standardization is perhaps

the most convenient and reliable monitor lead provided a central terminal with high resistors between the limbs is used.[71]

"Incomplete left bundle branch block" (initial right septal–late left mural activation) and an entity designated as "bilateral, incomplete bundle branch block" (initial right septal–late right mural activation) are described in detail, for the first time, in healthy young subjects. In both of these entities, a Q wave is present in right sided leads identical with that found with complete left bundle branch block.

The difficulty of differentiating between various types of intraventricular conduction and ventricular hypertrophy has been reviewed.

The similarity of electrocardiographic peculiarities in so called incomplete left bundle branch block and anteroseptal myocardial infarction has been emphasized. It appears that the diagnostic criteria of Wilson[1] for myocardial infarction remain the best means of avoiding misinterpreting peculiarities in intraventricular conduction as evidence of myocardial infarction.

A new nomenclature for the various types of intraventricular conduction is suggested. This nomenclature is purely descriptive and has, at present, the advantage of having no clinical connotation. It eliminates the requirement for making the often impossible differentiation between complete and incomplete bundle branch block. Similarly, this nomenclature simplifies the problem of differentiating between bundle branch block and those conditions that may not represent so called defects in intraventricular conduction but have similar electrocardiographic characteristics.

Finally, some of the limitations of present day clinical electrocardiography have been pointed out and thereby the need for further, precise investigation of electrocardiographic problems is implied.

The data on which the observations in this chapter are based were obtained with the aid of Dr. Harvey J. Breit, Dr. Sami I. Said, Dr. Mahdi Murtadha, Dr. Henry M. McLaughlin, Dr. Hai Byung Youn and Dr. Thomas M. Cook. Mrs. Anne Pearson made invaluable contributions in all phases of this work.

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11 The U Wave

CHARLES E KOSSMANN, M D

IN CHAPTER 1 brief reference was made to the terms prepotential negative after potential and positive after potential Each of these terms is used to describe a type of deviation during diastole of the polarized state of the membrane from the normal resting level (fig 1) The prepotential (Chapter 1 fig 6) is the gradual loss of polarization until threshold is reached and propagation begins which is characteristic of automatic tissue[1] Negative after potential and positive after potential are terms used to describe a deviation from resting potential occurring immediately after the phase of repolarization of the monophasic action potential In the former the gradient of potential across the membrane is incompletely restored (hypopolarization) in the latter the gradient is exaggerated (hyperpolarization) The terminology is confusing because the negative after potential is represented in the record of the intracellular potential as a plateau or summit—the interior of the cell is less negative by virtue of the incompleteness of polarization of the cell membrane By the same token however the outside is less positive (relatively negative) and if the monophasic action potential is recorded as an injury potential (Chapter 1 fig 2) the electrode on the exterior of the cell will in truth be more negative (less positive) than it would be with the cell completely repolarized

During the existence of a negative after potential the difference between it and the threshold potential is smaller than between the latter and the true resting potential It is at such time that the cell might be expected to show one type of supernormality Early in the relative refractory period there are relative periods of supernormality which result in dips of the strength interval curves (Chapter 15 and fig 4 Chapter 1)

Negative after potentials apparently occur normally in the MAP of the chick heart It appears to be the consensus at present that positive after potentials (hyperpolarization) occur only pathologically or artificially

MECHANISM OF THE AFTER POTENTIAL

Not too much is known of the actual mechanisms involved in the creation of after potentials In the prepotential of automatic tissue there appears to be a diastolic impairment of impedance of the membrane with a gradual disappearance of the ionic *gradient* until threshold is reached and a response propagated

It is known that during systole there is an efflux of potassium from the cell[2] This ion presumably returns during early diastole when an after

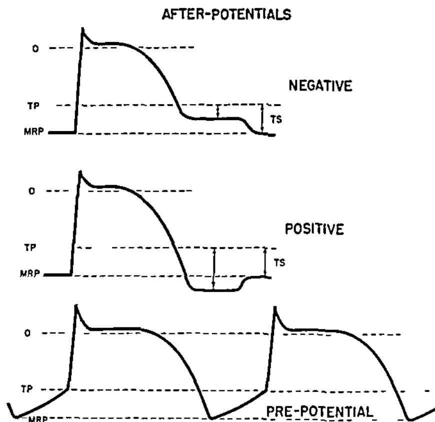


FIG 1 A diagram to illustrate the nomenclature of after potentials as seen in a record of the transmembrane potential MRP membrane resting potential TP threshold potential TS threshold stimulus O zero level of potential

potential, if present, is found It is conceivable that anything which hinders the return of potassium to the cell may impair the full development of the membrane resting potential [4] Conversely a temporary excess of intracellular potassium might result in a greater than normal MRP (positive after potential)

AFTER POTENTIAL AND THE U WAVE

Since indirect leading from the cell surrounded by a conducting medium yields a record, depending upon the location of the leads of the axial or membrane current (Chapter 4) and since these are respectively the first and second derivatives of the monophasic action potential [5] it follows that the final slope of the after potential may manifest itself in an indirect lead as a monophasic or diphasic deflection There is evidence too, to indicate that the duration of the action potential and probably of the after potential varies in different parts of the heart as does repolarization itself It would be expected, therefore that these differences would result in a

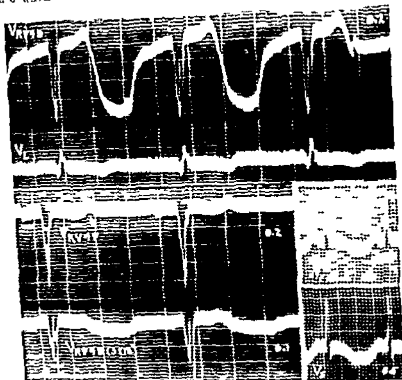


FIG 2 Intracardiac leads in a 28 year old negro male with heart disease of unknown cause displaying a large late negative potential possibly caused by hyperpolarization The upper record ($V_{RV\ D}$) from the right ventricle made simultaneously with the potential of the left arm (V_L) shows a spontaneous disappearance of the after potential at the end of the strip just as a calibration voltage was put into the circuit

The lower left records were made with a double electrode catheter in the right ventricle with the electrodes separated by 3 cm The proximal electrode recorded the probable true potential of the cavity ($V_{RV\ P}$) and the distal electrode recorded the negative after potential but in lesser degree than initially ($V_{RV\ D}$) The occurrence of the after potential near the end of the T wave and its persistence for almost 0 3 sec into the T P interval is to be noted The time lines occur every 0 2 sec

In the lower right hand corner are leads aV_F and V_4 in a 67 year old woman who had received quinidine for the treatment of atrial fibrillation in the preceding 24 hours A late downward deflection fused with the T wave and occupying the entire T P interval is to be noted The time lines in these records represent 0 04 sec String sensitivities are as indicated otherwise normal (From Hoffmann Ann New York Acad Sc 65 8 0 1957)

gradient of the after potential with effects on indirect leads similar to those observed with the T wave As will be seen this proves to be the case in clinical records the U wave tending to behave with certain exceptions to be noted much like the T wave

The tacit assumption made in the above statements is that the U wave is, in truth, the result of an after potential. Actually, this seems the most reasonable explanation at present, and subsequent discussion will be based on it. However, there is no universal agreement, and such causes as stretch of the ventricles in diastole ("distention potentials"), the long duration of the action potential in Purkinje tissue, and late excitation and recovery at the base of the interventricular septum (Chapter 10) have been advanced as causes. Data and reasoning can be advanced to refute all.[4, 6] Of interest relative to origin is that movement of the heart (relaxation) may occur at the time of the U wave since the isometric relaxation period ordinarily terminates 0.1 sec. after the beginning of the second heart sound or after the end of the T wave. In this connection, it is to be recalled that movement of the heart occurs between the approximate end of QRS and the beginning of the T wave.

A few interesting observations of possible fundamental significance have been made in this laboratory on the U wave. In an intracardiac lead a long, "positive" after potential was noted when pressure was made on the *endocardium of the right ventricle (fig. 2)*. Kleinfeld has obtained a similar record from the interior of the ventricular cell of a frog.

Clinical Aspects of the U Wave

It is general knowledge that measurements relative to the U wave are difficult to make at best. Making electrocardiograms at greater than the conventional paper speed and at higher than the usual gain may overcome some of these difficulties.

So far as its form is concerned the U wave is normally smaller than the T wave and, unlike the latter, has an initial rapid slope and a slower final slope. It is said to be identifiable in 85 per cent of extremity leads and 100 per cent of precordial leads, especially midprecordial leads.[4] On the average it is small (0.02 to 0.03 mv.) although occasionally in the chest leads a normal U wave of 0.2 to 0.3 mv. may be encountered. It tends to be high when the T wave is high, as in normal subjects in a good state of physical training. Its direction is usually upward except in those leads where an inverted T wave is normally encountered (leads V_R, III). In children, however, the U wave may be upright in leads from the right side of the precordium *with a normally inverted T wave, and this point is said to be* of use in differentiating such records from those in which there is right ventricular disease. The wave has a duration of 0.09 to 0.34 sec. and tends to be longer with slower heart rates.

Variations in *magnitude* of the U wave occur in a good many clinical conditions. It will often be high in the presence of left ventricular hypertrophy and in hyperthyroidism. Abnormalities in the concentration of serum

potassium affect the T wave and the U wave in opposite directions In hyperkalemia the T wave tends to be high and pointed and the U wave small in hypokalemia the T wave is decreased in size or inverted and the U wave exaggerated Surawicz and Lepeschkin[7] have fairly convincingly demonstrated that the prolonged Q T interval formerly ascribed to a low serum potassium is really a Q U interval mistakenly labeled

In view of what has been said above regarding the theoretical genesis of a negative or positive after potential the changes in the U wave noted in connection with abnormalities of serum potassium seem reasonable though unproven when stated in terms of the relative intracellular and extracellular concentrations of this ion In hypokalemia K readily leaves the cell during systole and returns slowly with a resultant large negative after potential and presumably U wave In hyperkalemia the return of K may be augmented with reverse effects on the parameters under consideration

Epinephrine calcium and digitalis augment the U wave but whether these are direct effects or indirect from altered permeability of the membrane to potassium is not definite Of interest is the failure of digitalis to alter the direction of the U wave

Drugs which augment the U wave in general increase the excitability of the heart This fits in well with the idea that a smaller diastolic threshold stimulus is required with the presence of a negative *after potential* but it is possible that this is not the whole story Lepeschkin[4] has stated that *quinidine acts* in an opposite fashion exaggerating the U wave but *reducing* excitability of the *ventricular muscle* ascribing the apparent paradox to an unusual elevation of the threshold by this drug One clinical experience with a 67 year old woman given quinidine for atrial fibrillation is shown in

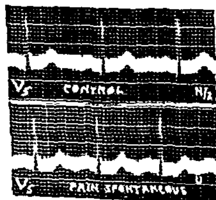


FIG 3 Lead V5 of a 43 year old white man with recurrent angina decubitus Above is a record made during an asymptomatic *period* Below is a record made during the spontaneous occurrence of pain In addition to a minor change in form of the T wave the latter also shows an inverted U wave

figure 2 In this instance the U waves became quite prominent and inverted Reasoning as above, this could mean the drug caused a large, positive after potential or hyperpolarization, and suggests that in this instance quinidine was operating, at least on ventricular muscle, to reduce excitability by increasing the density of charges on the membrane

A change in the *direction* of the U wave *occurs in a variety of situations* In normal subjects it can be inverted by intravenous norepinephrine In left ventricular hypertrophy it may be inverted in leads reflecting the surface of the left ventricle, and in right ventricular hypertrophy in leads from the right side of the precordium In myocardial infarction it will often be obscured early but after the initial effects on the S T segment and T wave disappear, an inverted U may remain The U wave may also become inverted in patients with anginal syndrome during a spontaneous attack (fig 3) or after a stress test [8]

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12 Electrocardiographic Effects of Myocardial Injury, Electric Images

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FROM THE electrocardiographic point of view injury may be defined as any process which completely abolishes or modifies singly or in combination the rate course or extent of the cellular membranous processes of depolarization repolarization or both [1] The definition in the broad sense includes injury to the conduction system and to automatic tissue although the following discussion will not be primarily concerned with these (see Chapters 10 15 16)

The electrocardiographic effects of injury to the myocardial cell have been summarized adequately in many texts and articles[1] These effects depend in general on the degree and the location of the injury relative to the recording electrode If injury is sufficient to cause anatomic as well as functional destruction of a part of the heart that part no longer contributes electrically to the total record and there will be alterations in the deflections resulting from excitation Depending on the orientation of the destroyed muscle within the heart to various surface leads an initial downward deflection or Q wave may appear However it is obvious from a consideration of mirror images (Chapter 5) that deflections of an opposite direction may be obtained in leads from the uninjured side of the heart Further it seems certain that injury can be of such nature as to cause a local slowing of depolarization (Chapter 7) which may result in a modification of its time-course and of the form and duration of the initial deflections resulting from this process[2]

The recovery process is affected by lesser degrees of injury which manifest themselves as abnormalities of the S T segment the T wave and the U wave The possibilities at the cellular level are

(1) That the cell is partially or completely depolarized at one site as a result of the injury The resting membrane potential of lesser magnitude in the injured area is electronegative with respect to the uninjured portion and a current of injury flows during diastole Being constant it causes no discernible displacement of the baseline of the recorder until depolarization during systole occurs Then the S T segment is displaced toward a zero level which would have obtained before the current of injury was introduced into the circuit

(2) The resting membrane potential is normal but injury prevents complete depolarization during systole In the injured region excitation is blocked and behaves like a charged lamina with its positive side

toward the injury An actual flow of current is produced, rather than abolished, during systole, with resultant displacement of the S T segment

(3) A combination of possibilities (1) and (2) is theoretically possible

(4) The after potential (Chapters 1 and 11) may be abnormal, resulting in a large, late negative deflection (inverted U wave)

(5) The rate of *repolarization or of its separate phases* (*Chapter 1*) may be changed These differences within the cell or in an aggregate result in a "gradient" in the rate of recovery, which is defined by the vectorial sum of the manifest mean vectors representing depolarization and repolarization It is obvious that there can be an atrial gradient (Chapter 8) as well as a ventricular gradient resulting from injury The significance of modifications of the U wave in calculation of the latter has not been evaluated

The mechanisms described above seem to be fairly well agreed upon The effects of pure subendocardial or pure subepicardial injury, so far as the regression deflections are concerned, also seem clear cut (fig 1A and C) A problem which has been disturbing for some time is the occurrence of elevation of the S T segment in an epicardial or precordial lead over a fresh transmural infarct Such an infarct usually has greater subendocardial than subepicardial dimensions The sum of the forces produced at the former boundary ordinarily would be larger than those at the latter and the two together should result in a downward displacement of the S T segment Bayley's[3] notion that the preservation of a subendocardial layer of intact muscle in transmural infarction accounts for the paradox may be true in some clinical instances but preservation of such a layer in the

A SUBENDOCARDIAL B TRANSMURAL C SUBEPICARDIAL

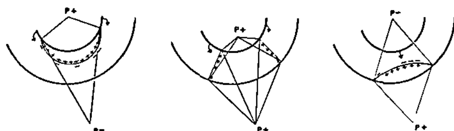


FIG 1 Diagram of the electrical effects of subendocardial transmural and subepicardial lesions The semicircles of different radii enclose a partial ring of cardiac muscle The stippled areas are dead muscle the clear areas *healthy muscle and* between the two is assumed to be an injured layer where excitation is blocked as it approaches from the endocardial surface (arrows) The variable electrical effect on points P inside and outside of the chamber are on the basis *of the relationship* $V = \phi\omega$ (Chapter 4 and Kossmann[11])

experimental animal[4] or in man is not essential for creation of the electric phenomena under discussion Pruitt and Valencia[4] have evidence that the S T elevation is present on both surfaces of a transmural lesion as a result of electric phenomena at the mural boundaries of the infarct and they point out that the magnitude of such boundaries is increased with ventricular systole when the S T segment is written (fig 1B)

Electric Images the Significance of Conducting and of Insulating Boundaries

With regard to the electric effects of injury on endocardial or epicardial surfaces of the heart a good deal of misunderstanding still exists compounded by the fairly recent observation of the absence of initial positive deflections normally and of S T displacements with injury in intramural leads made from the subendocardial layers of the ventricles One group of investigators[5] failed to obtain S T displacement in the cavity of a chamber but did get good reciprocal displacements of this segment on the epicardial surfaces over and opposite to a transmural infarct of the left ventricle in dogs Their explanation for the observation is not entirely satisfactory Actually a similar experiment was reported in 1948 by Pruitt and Valencia[4] and the results better explained by the method of images Because little attention has been paid by most investigators to the fact that in taking an epicardial lead from the exposed heart there are three media of different resistivities involved—the heart's blood the myocardium, and the external air—a consideration of these particularly in relation to myocardial injury seems indicated

A part of this problem in electrocardiography that is incompletely solved is the importance of the heart's blood in the determination of the magnitude of surface deflections It has been demonstrated that the blood's resistivity (specific resistance)* is about 200 ohm cm as compared to 800 ohm cm at one ke for myocardium and general body tissue 1000 ohm cm for lung and 1500 to 5000 ohm cm for fat[6] Experiments by Nelson and associates[7] suggest that the manifest heart vector may be reduced approximately 25 per cent by virtue of the short circuiting effects of contained blood This fits well with a fairly common clinical observation that the voltage of electrocardiographic deflections in a failing heart

* Resistance of a conductor is directly proportional to its length and inversely proportional to its area A constant ρ is characteristic for the material concerned so that the relation can be written $R = \rho \frac{l}{A}$ where l is the length in cm and A the cross sectional area of the material in cm The specific resistance then is $\rho = R\frac{A}{l}$ in ohm cm

dilated with sequestered blood, *is often lower than in the same heart* reduced in volume by appropriate therapy

Perhaps more significant from the viewpoint of interpretation is the effect on the electric phenomena observed when the medium to which the epicardium is exposed has a resistivity which is infinite. Most observations on animals and on man have been made with the heart exposed to air, only a few have been made with a medium of high conductivity covering the heart.[4, 8] Such differences in experimental procedure make for complexity of interpretation because the dissimilar densities of the electric fields in contiguous media result in electric images at the boundaries. These may augment or attenuate recorded voltages depending upon whether the source is in the medium of lesser or greater conductivity and upon the orientation of the electromotive force to the plane of the boundary.[9, 10] The magnitude of the image is also determined by the shape of the boundary.[10]

The concept of electric images* originated with William Thomson (Lord Kelvin[11]) and was simply compared to virtual optical images by his biographer, S. P. Thompson,[1] quoted by Hecht.[13] The analogy was given of the well known example of a candle in front of a mirror and its image, the same distance *behind the mirror giving the equivalent illumination of a* candle at each of these sites when the mirror is removed. When the candle is placed in front of a polished silver ball the image within the ball is smaller and nearer to the surface than the candle itself. Nelson[10] has reviewed and *checked the mathematics of the situation with the aid of a double layered* electrolytic tank[14] and shown the considerable effects of an insulating boundary (comparable to the body surface number 3 in fig. 1, Chapter 1) on the electric field of a dipole. Brody[9] on the other hand has brought out analytically the augmenting effect of the internal medium (number 4, fig. 1, Chapter 1) on electromotive forces normal to, and attenuation of those tangent to, a spherical conducting boundary such as approximately exists between the endocardium and the heart's blood.

The principles and formulations involved in the method of images where an injured surface of the heart is concerned are shown in fig. 2, which is modified slightly from fig. 5 of the article by Pruitt and Valencia.[4] The following is taken almost verbatim from their article. In the three parts of fig. 3, AB is a plane boundary between medium 1 (below) and medium 2 (above), with resistances k_1 and k_2, respectively. In medium 1 is a source of current at a distance a from the boundary. I in medium 2 at an equal distance b from the boundary is the image of the source S, in medium 1. Under the circumstances it can be demonstrated that the flow of current

* To be differentiated from image space and mirror images mentioned earlier (Chapter 5)

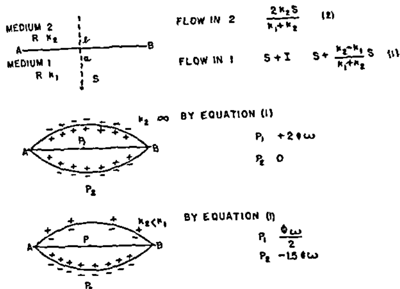


Fig 2 The method of image as applied to a problem of injury to the surface of an excitable tissue bounded in one instance (middle figure and equation) by an insulator ($k = \infty$) and in the other (lowest figure and equation) by a medium which conducts better than the excitable tissue itself ($k_2 < k_1$) Formulas for current flow in contiguous media are shown in the highest figure I image S source AB boundary k and k_2 resistances of contiguous media P_1 P_2 points in media ω solid angle subtended by a charged lamina on a sphere of unit radius at points P or P φ a constant defining the density of charges on the charged laminae (source of image) (Modified from Pruitt and Valencia Am Heart J [4])

at any point in medium 1 is the same as would be produced by the source S together with a source S $(k_2 - k_1)$ $(k_1 + k_2)$ placed at I if medium 1 were infinite in all directions rather than bounded The current at a point in medium 2 is the same as would be produced by a source $2k_2S$ $k_1 + k_2$ placed at S if medium 2 were infinite in all directions

When the second medium is a perfect insulator then k_2 becomes infinite and by the first equation the image at I becomes equal to the source at S and of the same sign In the middle part of fig 3 the source and image are shown as polarized surfaces The solid angle subtended by each at a point P_1 on the boundary is the same and the voltage at P_1 is $2\phi\omega$ or double what it would be if the medium surrounding the injured muscle were infinite in all directions On the other hand at point P_2 in medium 1 the solid angles are opposite in sign and the voltage recorded is accordingly zero

If the boundary AB is regarded as the epicardial surface of the heart

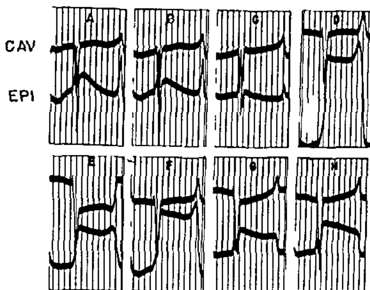


Fig 3 *Upper curves (CAV)* were recorded with an exploring electrode in the cavity of the turtle ventricle lower curves (EPI) with an electrode on or adjacent to the epicardial aspect of the ventral wall A control prior to immersing the dorsal surface of the heart in Ringer's solution B control after immersion of the dorsal surface *C control with ventral surface of the heart covered by a pad soaked in Ringer's solution* D after burning ventral surface of the heart lesion and ventral wall of heart exposed to air E immediately after D ventral surface of heart covered with a pad soaked in Ringer's solution F immediately after E pad removed from ventral surface of heart G *ten minutes after burn pad over heart* H immediately after G pad removed from surface of heart

Ordinate scale upper curves 5 mv /cm lower curves 3 5 mv /cm except when ventral surface of heart was covered by pad then 0 5 mv /cm (Pruitt and Valencia[4])

medium 1 as the myocardium and medium 2 as the surrounding air and if a source S is created by a burn on the epicardial surface the potential of a point on this freshly burned area during systole should be large The reason is that the most injured portion is not in contact with a conductor The electric field in the heart is thus incomplete (not short circuited') For the same reason a lead from the cavity corresponding to point P in that figure may not show any abnormality An exact and most illuminating experiment illustrating this was done by Pruitt and Valencia[4] with the turtle heart and the results are shown in fig 3

If the most injured portion of the burned surface is put in contact with the remainder of the heart by means of a cotton pad wet with *Ringer's* solution placed over it the potential of the burned surface will be reduced but the cavity potential during the inscription of the S T segment may be considerable This is exactly what happens as can be seen in fig 3 Returning to fig 2 for the explanation if the resistance of medium 1 is greater

than the resistance of medium 2 then by formula (1) the image is of the reverse sign tending to reduce the voltage of the source The situation is shown in the lower part of fig 2 in which the lamina representing the image has been assumed to have half of the charges of the lamina representing the source Under the circumstances the potential at P_1 becomes $\phi\omega/2$ and at P_2 it becomes $-1\ 5\phi\omega$ What the conducting pad does is to complete the field, and if large enough it may reduce the whole surface to an average potential approaching that of ground Not to be lost sight of is the fact that the image in the example given is reversed in sign (see below) The quantities given in fig 2 are of course assumed for purposes of illustration However mathematical rules are available for exact calculations[9 10 15]

A generalization of the method of images may be stated as follows With a source of current regarded as a charged lamina at the boundary of any given medium the potential of points between it and its image in a medium of higher resistance will be augmented and elsewhere in its own medium attenuated When the adjacent medium is of lower resistance the reverse effects on the potential of the points under consideration occur Whether the points will be positive or negative will depend on the orientation of the laminal charges with respect to the media

A simplified summary with the electric source (S) and image (I) in vector form for a plane boundary between media with resistances of k_1 and k_2 is shown in fig 4 The sources and images have been drawn of equal size simply for convenience the dimensions and relative conductivities of the media the location of the exploring electrode and the shape of the boundary (plane spherical irregular) in the biological system probably operate to make this equality an infrequent coincidence

Electric images are of particular importance when experiments are done on exposed hearts because in these experiments invariably one boundary of the heart is an insulator air Unless consideration is given to the image phenomenon some erroneous conclusions may be drawn regarding the distribution of potential differences *in the heart* especially those caused by injury[5] Clinical conclusions based on such misinterpretations of necessity are premature and probably faulty

Electric images have probably also been inadequately evaluated in the explanation of small R waves in intramural leads near the endocardium It is true that by the method of images there should be some augmentation of the R wave if the wave of excitation proceeds outward in normal fashion to the endocardial surface The ten times greater rate of conduction in the Purkinje system as compared to the ventricular myocardium makes it certain that some component of mural excitation is tangential to this surface and accordingly will be poorly recorded or not recorded at all

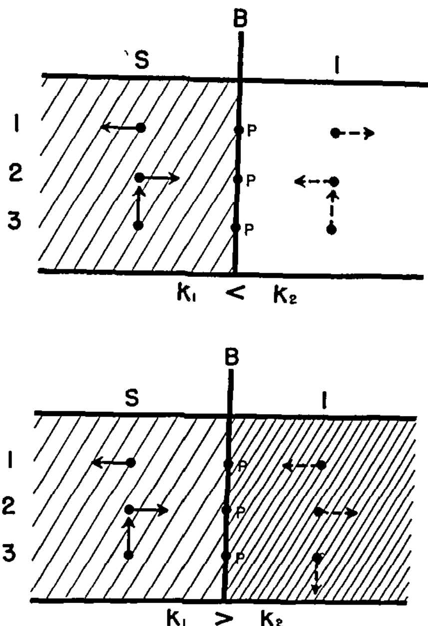


FIG 4 Diagram to illustrate qualitatively the images (I) of variably oriented dipole sources (S) near the boundary of a medium contiguous in the upper instance with another medium of greater resistance ($k_2 > k_1$) and in the lower instance with one of lesser resistance ($k_1 > k_2$) S source I image B plane boundary P points on the boundary equidistant in each instance from the source and the image

In the lower illustration simulating in a gross way the boundary between endocardium and heart's blood (right) it can be visualized how a lead made to the left of the sources would record augmented potentials if the dipole axis were normal to the boundary and attenuated potentials if the dipole axis were tangent to this boundary

The possible application of the method to this complex problem is cited simply to emphasize that the small or absent R wave in subendocardial leads may have explanations other than that the subendocardial ventricular muscle does not contribute to the electrocardiogram

Some Clinical Aspects of Myocardial Injury

The effects of injury on the initial and final atrial and ventricular deflections are well known and have been touched upon above Abnormal ectopic rhythms as a result of injury probably arise from impaired impedance of a cell membrane or group so that a prepotential (Chapter 1) develops during diastole which is sufficiently steep in slope to reach the threshold of the involved cells with discharge and propagation at a rate faster than that of the basic pacemaker

In the *atria* it is probable that injury is more frequent than suspected but is obscured by the fact that the final atrial deflections are simultaneous with the initial ventricular deflections and the displacements of the P R segment (S T_P) are not usually great (Chapter 8) The basis of this statement is that atrial infarction has been observed in 17 per cent of 180 cases of ventricular infarction by Cushing and his associates [16] Most often this is found in the right atrium in the region of the crista terminalis [16, 17]

The occurrence of S T elevation when pressure is made on the endocardial surface of the atria with a catheter-electrode has been of some value in the diagnosis of Ebstein s anomaly [18] If the catheter records an atrial pressure and the electrode pressed against the endocardium shows elevation of the S T segment rather than of the S T_P segment the likelihood is that ventricular muscle is making up part of the right atrial chamber The production of ventricular premature systoles in the same location with manipulation of the catheter is also good evidence of ventricularization of the right atrium [19]

In the *ventricles* pressure with a catheter may cause almost a monophasic record (ref 20 and fig 5) This can only mean that subendocardial muscle is as capable of contributing to electrocardiographic abnormalities as is any other layer The clinical counterpart of this type of touch potential or pressure potential in which excitation block rather than a current of injury is involved is a tumor of the heart or pericardium which makes pressure on normal myocardial cells or a ventricular aneurysm which produces tension on the normal cells at its margins as the aneurysm undergoes paradoxical pulsation during systole

A clinical problem which has been debated is the effectiveness of left bundle branch block in obscuring the electrical effects of left ventricular infarction Originally Wilson believed that this was true of QRS unless the interventricular septum was involved by the infarct Its effects on the S T

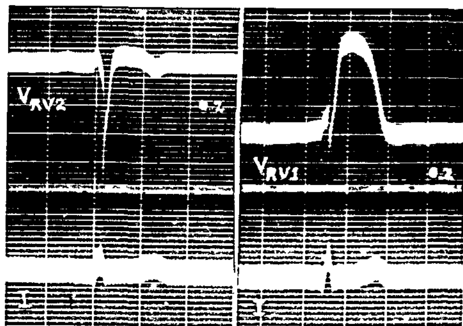


FIG 5 Leads from adjacent points in the right ventricle of a normal man showing the monophasic distortion which occurs (V_{RV1}) when the electrode makes pressure on the endocardium Time lines are 0 2 sec and the simultaneous lead is lead I (I) The figure illustrates that subendocardial muscle at least in the right ventricle behaves electrically as does subepicardial muscle when pressure is made on it (From Kossmann et al Circulation[20])

segment and T wave were not denied but it was believed that these could be determined only by measuring the ventricular gradient Kennamer and Prinzmetal[1] have obtained a lowering of left sided precordial R waves and S T segment displacements of the usual kind when left bundle branch block was produced following infarction induced with a tie on a coronary artery It has also been reported that changes in S T and T may be induced by exercise in patients with coronary stenosis and left bundle branch block [illegible] An occasional clinical example of myocardial infarction occurring in a patient with left bundle branch block will show abnormalities of the final ventricular deflections which appear to be dominated by the effects of the first mentioned lesion It is likely that this occurs particularly when the mean manifest spatial potential of the T wave is small to begin with despite the block

One type of record has caused some concern in regard to its anatomic and clinical significance It is characterized by no recognizable abnormalities of QRS but the T wave is deeply inverted principally in midprecordial leads and preceded in some by a depressed S T segment (figs 6 and 7) Papp and Smith[23] described this type of electrocardiogram in a paper on slight coronary attacks The title was chosen because in many instances the

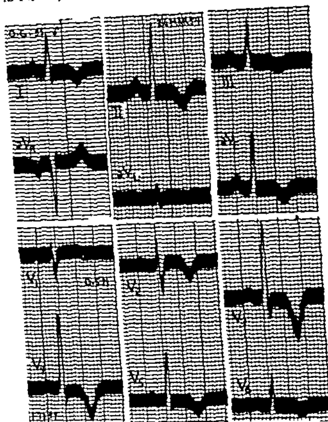


Fig 6 The bipolar (I II III) augmented unipolar (aVR aVL and aVF) and standard chest leads (V1 to V6) the latter recorded at half normal sensitivity of the galvanometer (1 mv = 0 5 cm) in a 53 year old white male admitted with cholecystitis and icterus In view of the electrocardiogram cholecystectomy was delayed for two month There was suspicion of myocardial infarction in 1952 but no cardiac symptoms since

abnormalities disappeared within a short time and the patient became asymptomatic Pruitt and associates [4] have described this in the course of coronary disease as well as in valvular heart disease in hypertensive heart disease both of the greater and lesser circuits in constrictive and calcific pericarditis [5] and in some patients believed to have no heart disease [4 28] Abnormalities of the S T segment are ascribed to subendocardial injury and the T wave inversion to transmural ischemia An example in figs 6 and 7 illustrates little change in this type of record over a period of three years in a man in his middle fifties The probable clinical significance of this type of electrocardiogram when it occurs in the course of coronary disease is that localized subendocardial necrosis

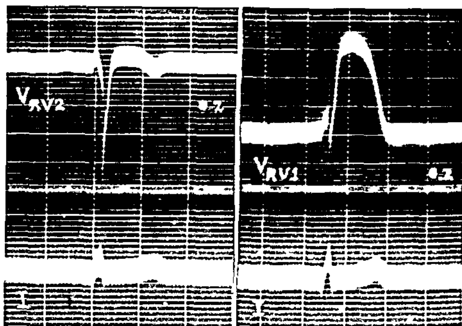


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of the displaced S T segment have been emphasized in several papers.[7,31] In particular they have pointed out the illusion of abnormal S T junction or segment depression after exercise caused by downward displacement of the P R segment (or T_P wave), the upward concavity of S T when displaced simply as a result of unusual decrease in the ventricular gradient of a rapid heart rather than from coronary insufficiency, the possible different effects on the spatial vectors in normal subjects of moderate aerobic, anaerobic and severe aerobic work, with changes in most of the measured spatial parameters (increase in magnitude and shift of T vector to the right, increase in the spatial angle between the QRS and T vectors) occurring with the last,[?] the change in QRS (decrease of spatial magnitude) with anaerobic work,[?] the inadequacy, in general, of the exercise tolerance test without adequate correlation with clinical data.

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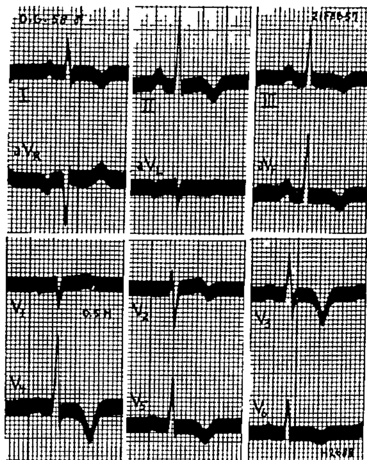


Fig 7 Electrocardiogram of same patient as in figure 6 recorded three years later The persistence of the abnormalities suggests that they are not on the basis of coronary disease

has been produced and in a majority of patients this is as far as the lesion will go when first seen However, it may also signify simply the early stages of a more extensive transmural infarct which may take hours to weeks to develop [6]

In Chapter 1 hyperpolarization was mentioned as a probable abnormal state of the membrane occurring in early diastole and corresponding to a positive after potential Unusual positive after potentials have been encountered with the intracardiac electrode[1] which promptly disappear when pressure on the endocardium is relieved They have also been seen with intracellular potentials They point up the likelihood that the U wave assumed to be related to after potentials, may be modified by injury (Chapter 11 fig 1)

The limitations of quantitative measurements of the S T segment and T wave in response to exercise and the considerable significance of the form

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13 Principles of Electrocardiographic Interpretation in Congenital Heart Disease

JOSEPH A. BRUMLIK, M.D.

Being aware of the limitations of electrocardiography, we do not assume that it will in itself provide a diagnosis in a case of congenital heart disease. Nevertheless, in any effort to solve an individual diagnostic problem presented by a malformed heart, an important source of information is missing if an electrocardiogram is not available.

As long as the pacemaker continues to be located in the sinoatrial node, the form of the atrial and ventricular complexes of the electrocardiogram is determined by the position of the heart, by the size, position and spatial relations of the individual chambers, probably by the thickness, absolute or relative, of the walls or their parts, by the state of the conduction system, by the general or local condition of the myocardium, etc. These factors apply to a malformed heart equally as to a heart affected by acquired disease.

Some malformations impose a heavy burden on the hemodynamic performance of the heart, e.g., the enormously increased blood flow brought about by an interatrial septal defect, or the triple or quadruple rise in ventricular pressure needed for overcoming the resistance of a stenotic pulmonary valve. In both instances it is mainly the right ventricle that bears the hemodynamic burden. Since the type of additional work constantly performed by the ventricle in the two conditions cited differs so widely, it can be expected that the ensuing anatomic adaptations of this chamber will diverge and that this divergence will find its expression in the form of the ventricular electrocardiogram (Chapter 14). Frequently there is a tendency for some malformations to display distinctive electrocardiographic patterns, but it must be emphasized that in any type of the ailments to be discussed there are variable degrees of severity, number of complications and at times exceptional features which influence and alter the form of the electrocardiogram. Recognizing this, the clinician should evaluate the electrocardiogram of a congenital cardiac lesion (as of any other cardiopathy) only in conjunction with the entire clinical picture and should not try to make an anatomic diagnosis on the basis of the electrocardiogram alone.

The great majority of malformations *per se* do not influence the electrocardiogram. It is the *consequences* of their existence that are apt to produce the changes in the electrocardiogram. Since the malformations are often complex and their effects on the heart multiple, the resultant electrocardio

gram easily becomes a problem in interpretation if one insists on identifying components supposed to correspond with distinct anatomic changes

Electrocardiographic and Vectorcardiographic Abnormalities When the Pacemaker Is in the Sinoatrial Node

The atrial complex may undergo the well known modifications when the pacemaker is in the sinoatrial node it may get taller, last longer, change its form, its mean axis may point outside the limits of the accepted normal It is generally agreed that a narrow, tall, peaked P wave means hypertrophy of the right atrium A large left atrium may find its expression in a broad (0 12 sec or longer), notched P wave in the bipolar extremity leads and in the prominent negativity of a diphasic (+ −) P wave in lead V_1[1]

Analysis of the ventricular complex is usually aimed at discovering signs of ventricular hypertrophy, either right or left, and separating them from signs produced by bundle branch block This endeavor is correct in principle and useful in practice However, the distinction between delayed conduction in a bundle branch and the effect of superimposed forces of hypertrophy cannot always be attained by simple means

Interpretation of the ventricular complex is commonly started by measuring its duration and by determining the angle of its mean electrical axis in the frontal plane The recognition of a prolonged QRS interval (beyond 0 10 sec in adults, 0 09 sec in children from 5 to 14 years old 0 08 sec in children under 5 years, measured in extremity leads) is easy but not too helpful in the differentiation of hypertrophy from incomplete bundle branch block precisely in the critical range between 0 08 or 0 10 and 0 12 sec (Chapter 10) From force of habit, one is inclined to equate right and left deviation of the electrical axis of QRS with right and left ventricular hypertrophy, and vice versa Though a homolateral hypertrophy and axis deviation may coexist such concordance is far from being the rule Less than two thirds of the patients with right ventricular hypertrophy present with right axis deviation and less than one fourth of the patients with left ventricular hypertrophy have left axis deviation [3] Thus the diagnosis of Fallot's tetralogy should not be discarded because there is no deviation of the electrical axis to the right similarly there is even less reason for rejecting the diagnosis of congenital aortic stenosis if the axis does not deviate to the left

For the electrocardiographic diagnosis of bundle branch block and ventricular hypertrophy, various criteria have been offered These sometimes widely differing standards must be kept in mind when comparing statistics about the incidence of electrocardiographic abnormalities in a specific type of cardiac malformation and in instances when an author has neglected to indicate which criteria he has adopted for their recognition

The classification of ventricular hypertrophies and bundle branch blocks we have used in this Chapter is that of Wilson, Rosenbaum and Johnston[4] and of the Subcommittee on Criteria for Electrocardiographic Diagnosis of the New York Heart Association. We are convinced that the following descriptions given by Wilson and his associates are the most reliable to date.

A pronounced right ventricular hypertrophy is characterized by a large R with a late peak, frequently preceded by a Q and followed by an inverted T in leads from the right side of the precordium (V_1, V_E, and often V_2); in leads from the left side R is often unusually small, early, and Q is absent.

In left ventricular hypertrophy the R waves in V_5 and V_6 are abnormally late and tall, preceded by a Q in one half of the cases and very often followed by an inverted T wave; on the right side of the precordium the normally small R in V_1 and V_2 is even smaller and the normally large S still larger.[4]

Biventricular hypertrophy is diagnosed by some authors[5, 6] on an empirical basis if, with signs of right ventricular hypertrophy in the right precordium (high voltage of the R wave, delayed intrinsicoid deflection, small or no S wave), the expected configuration of the QRS complex in the left precordial lead (low R, deep S deflections) is absent and instead a tall R wave, sometimes preceded by a Q deflection and followed by a small or no S deflection, makes its appearance.

Incomplete right bundle branch block can be justifiably diagnosed when with a QRS wider than 0.08 sec. there is a secondary R in both V_1 and V_E. When the R' is small and confined to V_1, the presence of a conduction defect in the right bundle branch is doubtful.[4]

Wilson and associates[4] consider the diagnosis of *incomplete left bundle branch block* difficult. "Neither the complexes of the limb leads nor those of the precordial leads can be distinguished from the complexes seen in many cases of left ventricular hypertrophy."[4]

As far as *complete bundle branch blocks* are concerned, we have adopted the criteria of the New York Heart Association, which characterizes these conduction defects as follows: A wide or notched QRS of a duration of 0.12 sec. or more with a late intrinsicoid deflection 0.04 sec. or more on the right side of the precordium in case of a right bundle branch block and

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0 06 sec or more on the left side of the precordium in case of a left bundle branch block"

The knowledge of electrocardiographic manifestations of right ventricular hypertrophy has been advanced by two contributions one[7] emphasizing an overlooked electric sign of this hypertrophy, and the other[3, 8, 11] offering a subtler differentiation between right bundle branch block and the homolateral ventricular hypertrophy which, as noted earlier, is often a difficult task for the electrocardiographer

Myers[7] has directed our attention to what happens in right ventricular hypertrophy if the ventricular septum is activated from right to left, an exception which—as has been demonstrated by the registration of intracavitary potentials—occasionally occurs in patients with right ventricular hypertrophy *The result is a deep Q wave followed by a tall R in right precordial leads*, especially in lead V_{3R}, in lead V_1 there is a QS complex with a notch on the downstroke, and in leads from the left precordium there is no Q wave but an RS complex (Chapter 10) Such electrocardiograms might be diagnosed as incomplete right bundle branch block with anteroseptal infarction rather than right ventricular hypertrophy if the existence of the latter is not considered[7]

According to Grishman and his group[3, 8, 11] recording of the horizontal projection of the spatial vectorcardiographic QRS loop may be of considerable use In right ventricular hypertrophy the loop, when viewed from above, rotates clockwise, i e , with the returning portion of the loop anterior to the *initial segment* In contrast all other conditions, except *left bundle* branch block display a counterclockwise rotation Grishman and his associates also stress that the RSR′ complex seen in lead V_1 and currently attributed to incomplete right bundle branch block can result not only from this disturbance in conduction but also from right ventricular hypertrophy (and also can be produced by the electric activity of a normal heart) *

In order to show two positive deflections with a negative excursion between them (RSR′ rsR′ rSR′ rSr′) in lead V_1 the vector loop has to touch twice and twice cross the zero axis of this lead and so produce two lobes on the positive and one on the negative side of the vector axis (fig 1) The sense of the *vector rotation and the form of the loop are irrelevant for* the resulting configuration of lead V_1 as long as the projections on the line uniting the point C_1 with the supposed center of the equivalent heart dipole remain the same In other words exactly the same M (RSR) form

* This reasoning is correct if the scalar lead V_1 corresponds to nothing else but the projection of electrical forces of the horizontal vectorcardiogram on the axis of this lead as first pointed out by Duchosal and Sulzer[14] and if the method of recording furnishes true rectilinear projections of the spatial vectorcardiogram (see Chapter 6)

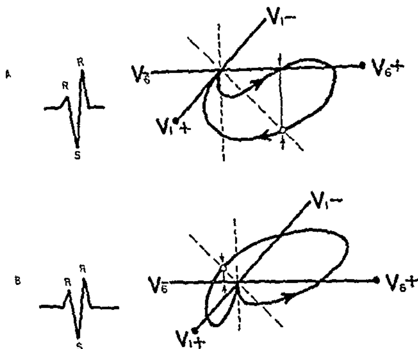


Fig 1 The drawing shows two ventricular complexes of identical (RSR′) configuration in lead V reflecting a projection (on the axis of this lead) of two horizontal vectorcardiographic loops of different shape and rotation The upper loop with its clockwise rotation (when viewed from above) is considered to be characteristic of right ventricular hypertrophy the lower rotating in a counterclockwise direction and displaying the anteriorly oriented terminal appendage is seen in instances of right bundle branch block The solid lines labeled V and V represent the axes of these leads the dots at one end of each axis the site of the electrode The dashed lines perpendicular to the axes divide the horizontal plane into two halves for each lead one of positive and the other of negative projection respectively The points on the loop marked by an open circlet correspond with the onset of R in lead V The points of their projection on the axis of lead V has been used by Schultz for the differentiation of right bundle branch block from right ventricular hypertrophy in electrocardiograms yielding an RSR′ complex in lead V If the projection of this point falls on the positive side of the axis of lead V corresponding with the R deflection in this lead (upper tracing) the RSR′ complex in lead V indicates hypertrophy If the projection of the point falls on the negative half of the same axis (lower tracing) right bundle branch block is implied Schultz procedure using simultaneous leads obviates the necessity of registering or constructing a vectorcardiogram for the identification of the two entities (see fig (Modified from Sapin Donoso Braunwald and Grishman)

of QRS in lead V_1 may correspond to various horizontal QRS loops produced by either one or the other sense of the rotation of the vector and be an expression—in the present state of our knowledge—of a normal electrocardiogram, right ventricular hypertrophy, or right bundle branch block. The characteristic trait of right bundle branch block is the terminal segment (fig 1), which usually assumes an appendage like shape, is inscribed slowly, and invariably appears oriented to the right and anteriorly.[1] It 'may coexist with any normal or pathologic variety of the QRS spatial loop.'[13]* Figure 1 shows that on the horizontal loop the point responsible for the onset of R' in lead V_1 (marked by a small circle) corresponds with a point on the *positive* side of the lead V_6 axis (R wave) in right ventricular hypertrophy but with a point on the *negative* side of the same axis (S wave) in right bundle branch block. This difference was used by Schultz[16] in this laboratory to distinguish these two abnormalities. His method requires simultaneous recording of leads V_1 and V_6 at a fast paper speed but dispenses with vectorcardiographic registration.

With these introductory remarks, we can proceed to the use of the *principles* set forth above for the study of the electrocardiograms encountered in congenital heart disease.

The *atrial wave* and the implications conveyed by its deformation have been mentioned. White and Burwell[17] many years ago described a tall peaked P wave in bipolar limb leads in pulmonary stenosis. Such P waves are seen especially in leads II and V_1 in instances of right atrial hypertrophy, dilatation, or both caused by increased atrial pressure flow, residual volume or other factors. According to Neill and Brink[18] a high peaked P wave when found together with a pulsating liver in cases of tricuspid atresia indicates a *small* interatrial septal defect, i.e. an obstacle in the only outlet for venous blood. Kjellberg and associates[19] and Van Lingen and Bauersfeld[20] emphasize the frequent occurrence of tall P waves in Ebstein's anomaly. As a matter of fact, the voltage of the peaked P wave may be so high as to simulate the initial deflections of the ventricular complex (fig 2), especially in right precordial leads. The absence of the described abnormalities of the P wave does not, of course, exclude the existence of anatomic alteration of the atrium.

The modifications of the P wave attributed to left atrial enlargement are seen in atrial septal defects, ventricular septal defects[1] and in cases of patent ductus arteriosus if accompanied by left ventricular hypertrophy.

The direction of the mean axis of the P wave as projected on the frontal plane assumes considerable interest in congenital malpositions of the heart.

* This implies that the right bundle branch block may be present with or without a counterclockwise rotation of the horizontal QRS loop.

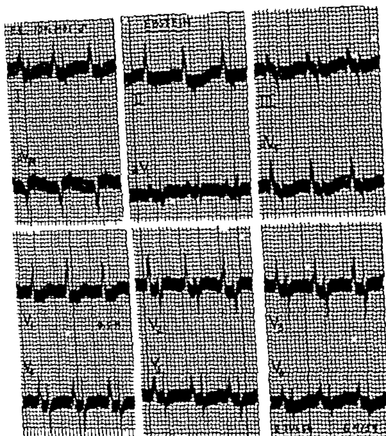


FIG 7 F I male 10½ months Eb tein s malformation (necropsy) The relatively narrow peaked high voltage P waves followed by a prominent T_P always oriented in th oppo ite direction e pecially in the right arm lea l and in the leads from the right precordium point to an enlarged right atrium The left deviation of the electri al axi of QRS angle alpha −60) and the diminutive size cf QRS in lea l V_1 ugg t a reduced *electrical* contribution by the right ventricle (ee also fig 1a)

in the chest Campbell and associates" s ummarize the situation as follows in dextrocardia with itus inver us (whether uncomplic ated or accompanied by a heart malformation) P in *lead I* is inverted that i its mean axis lies around the +120 direction (mirror picture of the normal axis with an angle alpha of about +60) In i olated dextrocardia despite the invariably present complicating malformation the P wave in lead I is generally upright corre ponding with a normal P axis In i olated levocardia i e in patients with a normally loc ated heart but with ubdiaphragmatic heterotaxy (who practically always display a evere cyanotic

malformation of the heart), the mean axis of the atrial wave, most characteristically manifested by the direction of the P wave in lead I, indicates the location of the venous atrium (together with the superior vena cava) if the P is inverted, the venous atrium is on the left side, if upright a right sided *venous atrium can be expected (fig 3)*

The size, duration, orientation in space, and form of the ventricular

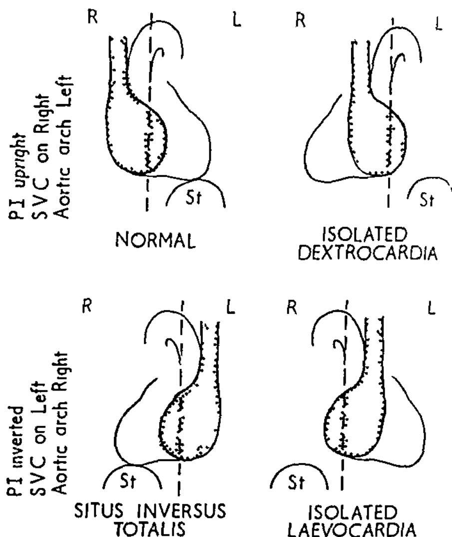


FIG 3 Diagram showing the effect of the position of the venous atrium (shaded together with the superior vena cava) on the direction of the P wave in lead I If the venous atrium is *in the normal position (normal heart isolated dextrocardia)* the P wave in lead I is positive if these structures are transposed (situs inversus isolated levocardia) the P wave in lead I is negative The aortic arch is usually opposite to the side of the venous atrium R right L left St stomach P I P wave in lead I (From Campbell and Reynolds Brit Heart *J*[22])

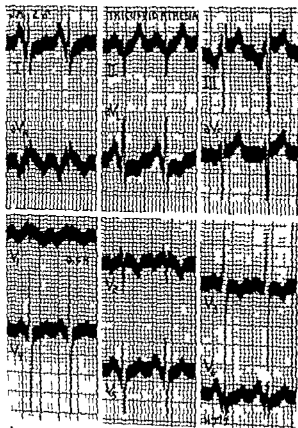


FIG 4 M male 9 years Tricuspid atresia pulmonary atresia atrial septal defect small ventricular septal defect atrophy of right ventricle considerable enlargement of the left atrium (ne rig v) The P wave of high voltage and of increased duration (leads I and aVL) is ascribed to hypertrophy of both atria Left deviation of the electrical axis of QRS is found in the majority of patients with tricuspid atresia Low voltage of QRS in lead V seem to be peak right ventricular atrophy similar to instances of Ebstein s malformation (However compare with fig 8 which shows a diminutive QRS complex in lead V_1 in the presence of right ventricular hypertrophy) A diphasic QRS occurs in lead V_3 and V despite right ventricular atrophy

complex depending on the configuration position and sense of rotation of the spatial vectorial loop offer a number of varied items of information which can be used with advantage in making the diagnosis

The electrical axis of the QRS complex as projected on the frontal plane may describe any angle with the *horizontal* (zero line) in heart malformations taken as a whole The *fallacy of identifying the deviation of this axis with homolateral hypertrophy* has been mentioned However it is a fact

that in the cyanotic group, a right deviation of A_{QRS} ($\bar{A}_{QRS}^{xy}$) is a rule and left deviation, which has been considered pathognomonic of, and uniquely occurring in, tricuspid atresia, an exception Though it is true that deviation to the left occurs very often in this malformation (fig 4), with more experience it has become known that not all cases of tricuspid atresia show it and, conversely, that there are a number of cyanotic cardiac malformations other than tricuspid atresia which may demonstrate left deviation of the electrical axis Fallot's trilogy, tetralogy, and pentalogy Fallot's tetralogy combined with a patent ductus, atrial septal defect, Eisenmenger's complex, single ventricle (fig 5), partial transposition of the great vessels with pulmonary stenosis, complete transposition of the great vessels, truncus arteriosus, patent ductus arteriosus with reversed flow infantile type of aortic coarctation, aortic atresia, Ebstein's malformation (fig 2), congenital fibroelastosis, and cardiomegalies of undetermined origin [13, 5, 6] The extreme deviations principally to the right (minus 180° to minus 60°), according to Sodi Pallares and Marsico [7] are seen in Fallot's tetralogy and pentalogy but never in pulmonary stenosis and Fallot's trilogy On the other hand, Brink and Neill, [5] in an unusually rich mate



Fig 5 A C female 5 months Small nonfunctioning left ventricle high in outflow tract atrial septal defect (essentially single atrium) agenesis of mitral valve pulmonary artery and aorta come from right ventricle (necropsy)

The electrocardiogram displays a left deviation of the electrical axis and diphasic precordial leads in the presence of a diminutive nonfunctioning left ventricle Note that the peaks of QRS complexes are not synchronous in the simultaneous precordial leads The latter were recorded simultaneously (upper right) and singly (below) at a calibration of 1 mv = 0 5 cm Time lines 0 04 sec

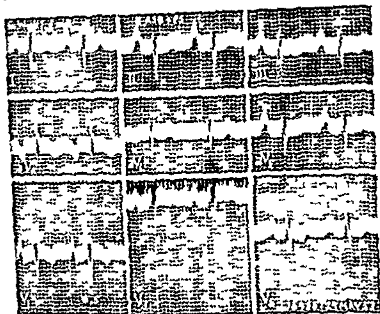


Fig. 6 G. W., male, 40 years. Fallot's trilogy: infundibular and valvular pulmonary stenosis with a wide atrial septal defect and massive hypertrophy of the right ventricle (necropsy). The P wave deformity (high and peaked in leads II and aVF) points to hypertrophy of the right atrium. The extreme right deviation of the electrical axis of QRS in the frontal plane (angle alpha about −150°) is unusual and its existence is even denied[77] in Fallot's trilogy. Notwithstanding the massive right ventricular hypertrophy and systolic overload (Chapter 14) the R waves in the right precordium are small and the T waves are inverted in leads V_1 and V_2.

mal found with extreme right deviation even in the two last named malformations (fig. 1). In the opinion of Donzelot and associates[78] a deviation of such proportions indicates massive right ventricular hypertrophy.

The occurrence of high voltage of the QRS complex in the bipolar extremity leads of some patients with congenital heart disease was first pointed out by Lewis[2] and pulmonary stenosis is mentioned in this connection. An initial ventricular complex far in excess of the upper limit of normal (2.5 mv.)[1] has also been found with interatrial and interventricular defects and with complete anomalous pulmonary venous return (fig. 7).

A decrease in the voltage of the QRS complex and especially of the R wave in lead V_1 was described following valvulotomy in some cases of pulmonary stenosis[79,80] and a similar change also was seen following the Blalock-Taussig operation in one instance of Fallot's tetralogy (fig. 8).

The classic electrocardiographic signs of right ventricular hypertrophy are helpful in the recognition of lesions that lead to an increase in the muscular

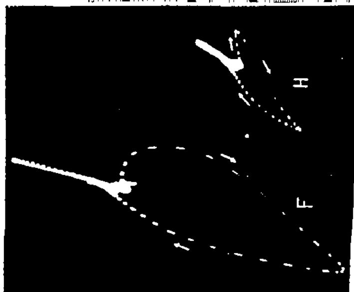


Fig 7 See legend on facing page

mass of this chamber Perhaps they are most marked in pure pulmonary stenosis or the closely associated Fallot's trilogy these being lesions accompanied by the highest known degrees of right ventricular hypertension and hypertrophy * Minimal and moderate stenosis, although invariably characterized by a significant gradient between the right ventricle and pulmonary artery may present a completely normal electrocardiogram [7]

Other important congenital heart diseases leading to this type of right ventricular hypertrophy and possible electric manifestations of it are Fallot's tetralogy and pentalogy persistent truncus mitral atresia transposition of the great vessels and exceptionally, interatrial septal defect persistent ostium atrioventriculare commune Ebstein's malformation tricuspid stenosis and fetal type of coarctation of the aorta

Similar signs of right ventricular hypertrophy are also seen in the patent ductus accompanied by pulmonary hypertension the latter evidently being the cause of the right ventricular hypertension and hypertrophy Cabrera and Monroy[34] have pointed out that the tracings of these patients in addition to a high R display an inverted T in V_1 and a high R wave on the left side of the precordium followed by a positive T wave Although not all patients with the reverse ductus present this type of electrocardiogram and in spite of the fact that these electrocardiographic changes are not the monopoly of the patent ductus with pulmonary hypertension, the empirical observation of Cabrera and associates[34] is correct (fig 9)

Donzelot [n] following Cabrera and Monroy's initiative * described a so called barrage (barrier) type of electrocardiographic right ventricular hypertrophy occurring in pure pulmonary stenosis (with or without interatrial communication) It is characterized by right deviation of the electrical axis of the QRS complex in the extremity leads negative T in leads aVF II and III tall R in right precordial (from V6R on) and mid precordial leads transitional RS complex shifted to somewhere between positions C3 and C5 T inverted and deep in right precordium mid precordium as far as position C4 and even C6 and C8 Miller reports that in 400 verified cases of Fallot's tetralogy this type of tracing has not been found once

Fig 7 (*facing page*) A M male 30 years Complete anomalous pulmonary venous return atrial septal defect pulmonary hypertension (diagnosed from signs angiocardiography and cardiac catheterization) The notched high prolonged P wave with a vertical axis suggests bilateral atrial hypertrophy though the radiologic examination demonstrated enlargement of the right atrium only The rsR in leads V_1 and V_2 can be interpreted as indicating either incomplete right bundle branch block or right ventricular hypertrophy The vectorcardiographic QRS loops (upper left) rotate clockwise both in the frontal (F) and horizontal (H) projections (reference frame Duchosal's tetrahedron) Clockwise rotation in the latter favors right ventricular hypertrophy and so does the simultaneous registration of leads V and V_4 (lower right) These demonstrate simultaneity of the onset of R in lead V_1 with the descending limb of the R wave of lead V Time lines 0 04 sec (Figure prepared by Dr Stanley Schultz)

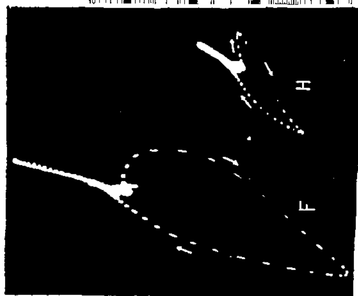


Fig. 7. *See legend on facing page*

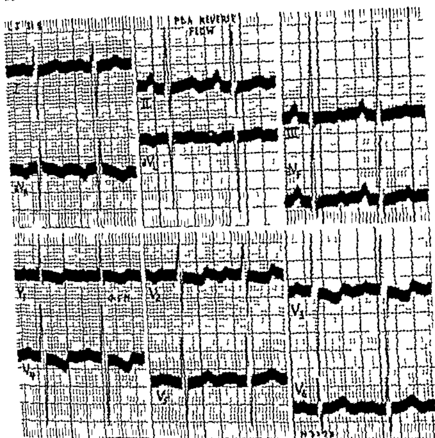


FIG 9 1 J female 31 years Patent ductus arteriosus with reversed flow (possible coexistent ventricular septal defect) Blood pressure brachial artery 114/70 mm Hg right ventricle 115 10 mm Hg pulmonary artery 110/75 mm Hg Oxygen saturation brachial artery [illegible] per cent femoral artery [illegible] per cent The brief duration of QRS (0 08 sec) the increased voltage of the R wave and the delayed intrinsicoid deflection in lead V can be considered as signs of right ventricular hypertrophy Tracings of this type with right deviation of electrical axis large R waves in all precordial leads and diphasic QRS complexes in midprecordial leads are considered by some to be characteristic of biventricular hypertrophy which is probably present in this case (compare with fig 13 which bears similar traits but without large diphasic or triphasic complexes in the precordial leads)

aortic root are characterized by a high R wave very often with a slur in its initial portion and a delayed intrinsicoid deflection over the right precordium (2) in contrast the hypertrophy of the right ventricle seen in interatrial septal defects most often displays the RSR configuration in position C_1 and thereabout

It comes to mind that the two forms of electrocardiographic manifesta

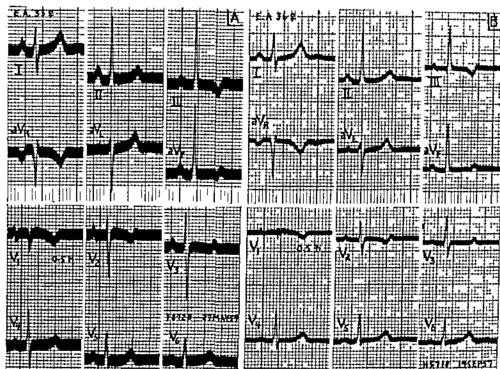


Fig 8 E A female 36 years Tetralogy of Fallot (confirmed by cardiac catheterization and thoracotomy) A A few days before operation (age 33) B Three years after a successful Blalock Taussig operation The P wave is less peaked the axis of QRS has shifted to the left about 15 but in general the changes are slight In either tracing there was little to indicate the right ventricular hypertrophy which was undoubtedly present in view of the patient's age and high intraventricular pressure (101/2 mm Hg)

It has been confirmed by other writers and has been established as useful in the diagnosis of patent ductus which, in these cases often is not easy to make Whether the picture of high R waves in all precordial leads with negative T waves on the right and positive on the left is due to the coexistence of left diastolic and right systolic overload [34] or to bilateral hypertrophy of the ventricles [5, 6] or to something else, remains to be proven We, as well as others, have observed similar tracings with ventricular septal defect and aortic coarctation

Grishman and his group[3, 8, 14] have pointed to the fallacy of diagnosing right bundle branch block just because there is an M (RSR′) form of QRS on the right side of the precordium and have shown that this pattern can be the result of right ventricular hypertrophy (fig 1) Clinically two old empirical observations retain their value for the differential diagnosis (1) the overwhelming majority of cases of right ventricular hypertrophy accompanying Fallot's *tetralogy or pure pulmonary stenosis is with normal*

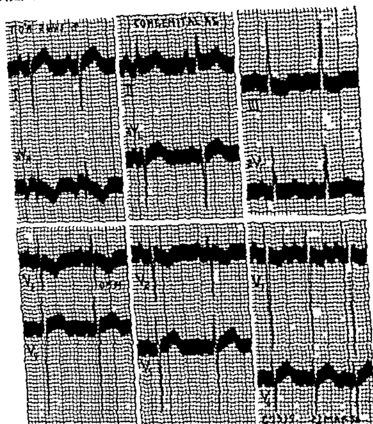


Fig 10 T O N male 2 weeks Congenital aortic stenosis bicuspid aortic valve (necropsy) In spite of a very tight aortic stenosis (orifice 1 mm) the electrocardiogram is within normal limits for the patient s age

resulting from this fistula and has revealed the unsuspected pulmonary hypertension that exists in a good number of instances The electrocardiograms may display wide interindividual differences The effect of an uncomplicated patency of the ductus is left ventricular hypertrophy which electrocardiographically shows the usual signs or remains silent How the added pulmonary hypertension especially in its severe form affects the electrocardiogram has already been mentioned Statistics on the form of the electrocardiogram in the patent ductus are rather incongruous It seems that in countries with elevated altitudes the percentage of normal electrocardiograms is low and the incidence of pulmonary hypertension with the resulting effect on the electrocardiogram high

Another malformation which may produce signs of left ventricular hypertrophy is the interventricular septal *defect* However in the majority

tions of right ventricular hypertrophy may originate in two differing anatomic forms of hypertrophy, one resulting from the task of overcoming the obstacle ahead and the other from the work of propelling the highly increased volume of returned blood. Kossmann and associates[36] expressed the conviction about the possible responsibility of the hypertrophied crista supraventricularis for the late R or R′ in leads from the right precordium (Chapter 9). Kjellberg[19] explains the differing mechanical response of the right ventricle to these two heterogeneous exigencies in the following manner: "When there is increased diastolic filling of the ventricle it is mainly the crista supraventricularis and its two bands as well as the trabeculae which hypertrophy. Hypertrophy of the actual ventricular wall takes place when the ventricle is forced to work under an increase of pressure." It has always been hard to understand why dilatation and/or hypertrophy of the right ventricle resulting from the altered hemodynamics of interatrial communication and functionally similar lesions should produce a bundle branch block. The notion that the M form of QRS, so often encountered over the right precordium in this group of heart malformations and commonly ascribed to a bundle branch block, may be just an expression of ventricular hypertrophy is strongly appealing to any worker in this field, but the genesis of the incontrovertible, complete right bundle branch block in these cases still remains obscure.

An important point should be kept in mind: the position of the heart in the chest,* especially by virtue of the counterclockwise rotation around the longitudinal axis, can nullify and even reverse the effect of right ventricular hypertrophy on the electrocardiogram.[37] In such cases a spatial vector cardiogram might be of considerable help in diagnosis.

Electrocardiographic signs of *left ventricular hypertrophy* are found in lesions taxing the left ventricle by increase either in the resistance situated ahead or in the volume of blood that has to be ejected. Examples of the former are aortic stenosis, subaortic stenosis or aortic coarctation; of the latter, patent ductus or septal defects with predominant venoarterial shunt. Despite left ventricular hypertrophy, the electrocardiographic signs of it are more conspicuous by their absence than presence, as is also the left deviation of the electrical axis (fig. 10).[3, 19, [illegible], 41] The T wave, however, may be inverted in all bipolar limb leads, especially in aortic stenosis,[41] with no deviation of the initial ventricular complex.

Among the congenital heart lesions that may cause left ventricular hypertrophy the patent ductus arteriosus occupies a position somewhat apart from the others. Why this is so has become clear only since cardiac catheterization has permitted a better insight into the hemodynamic alterations

* As a matter of fact, the electrical position of the heart is horizontal in the majority of cases of congenital heart lesions.[15, 35, 40]

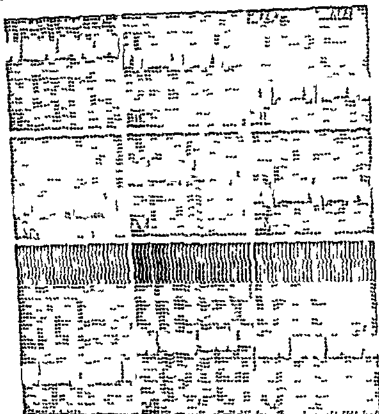


Fig 11 J A male 2 months Pulmonary atresia patent foramen ovale patent ductus arteriosus hypertrophy of both ventricles especially the right dilatation of the right atrium (necropsy) Right atrial hypertrophy may be suspected from the high voltage peaked P waves in leads II III and aVF Right deviation of the QRS axis is normal at this age The diphasic QRS complex in the precordial leads possibly favors the diagnosis of ventricular septal defect

ventricular wall We can confirm the correctness of this clinical observation (fig 15)

In heart malformations *left bundle branch block* is a rarity found occasionally in patients with tricuspid atresia [19, 51] anomalous coronary arteries [52] congenital fibroelastosis [47] Ebstein's anomaly [48] and single ventricle [18]

It might be expected that bundle branch block or even A V block would accompany complete defects of the ventricular septum (trilocular and bilocular hearts) but this is by no means so (fig 16) [18, 54] The absence of the septum usually does not modify the ventricular complex in any striking manner and even the Q waves ascribed as a rule to septal depolarization

of cases these signs are not present and the electrocardiograms are either within normal limits or they assume other forms, of which two have some diagnostic importance. First, the large diphasic ventricular complexes occurring in at least two bipolar extremity leads ("Katz Wachtel phenomenon")[43] are rather characteristic but they appear rarely in extremity leads and may also be seen in other congenital cardiopathies: mitral atresia,[41] trilocular biventricular heart, single ventricle,[15, 44] bilocular heart, transposition of the great vessels, aortic stenosis, coarctation of the aorta, von Gierke's disease, and atrial septal defect.[18, 19, 45, 46] In Burchell's opinion,[44] this phenomenon is especially prone to appear if both ventricles are equally thick or if there is just one ventricle. These diphasic complexes are not uncommon in unipolar precordial leads (fig. 11). Second, a morphology resembling the one mentioned in connection with patent ductus complicated by pulmonary hypertension has been described in ventricular septal defects: large R waves in all precordial leads with inverted T waves on the right, upright on the left. The S waves are said to be deeper in leads V_2 to V_4, and the deep Q waves in leads V_5 and 6 are attributed to the unusually strong, initial septal vector resulting from hypertrophy of the ventricular septum.[1]

Exceptionally left ventricular hypertrophy may become manifest in the electrocardiogram of atrial septal defects especially when combined with another malformation such as aortic stenosis* or atrioventricularis communis. In infants it has been reported in instances of fibroelastosis[47] and von Gierke's (glycogen storage) disease.[31]

Right bundle branch block, complete or incomplete, the significance of which was discussed at some length above, is encountered not only with the interatrial septal defect[49] (figs. 12 and 13) but also with anomalous pulmonary venous return, a malformation engendering hemodynamic changes analogous to atrial septal defect (fig. 7). It has also been found in ventricular septal defect (fig. 14), patent ductus arteriosus and Fallot's tetralogy, and its relatively high incidence in coarctation of aorta surprised a number of authors.[19, [illegible], 50] A special form of right bundle branch block has been described by Kjellberg[19] and by Van Lingen and Bauersfeld[50] as occurring in Ebstein's anomaly. It shows the usual general outline and duration ((0.12 sec. or more), however, the voltage of the ventricular complexes obtained in leads from the right precordium (V_1 to V_3 or V_4) tends to be smaller than normal, while it is of average amplitude on the left side. The low voltage is attributed by the authors to the thinness of the right

* Left ventricular hypertrophy is by no means the rule in this combination: we had under our observation a case of interatrial septal defect with subaortic stenosis (woman, 48 years, autopsy) whose electrocardiogram showed signs of right ventricular hypertrophy.[48]

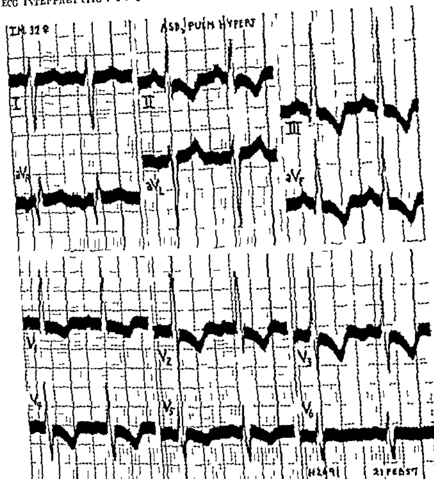


FIG 13 I M female 37 years Atrial septal defect pulmonary hypertension (diagnosis from signs and cardiac catheterization) Blood pressure brachial artery 99/75 mm Hg right ventricle 80/5 mm Hg pulmonary artery 80/43 mm Hg The delayed onset of the intrinsicoid deflection and the rsR's in lead V_1 with a duration of 0 11 sec can be ascribed to right *ventricular hypertrophy* or to incomplete right bundle branch block The form of QRS in lead V_1 resembles the QRS in figs 7 9 12 14

if one coronary artery usually the left or both coronary arteries arise from the pulmonary artery as first noted by Bland and associates [56] There are abnormal Q waves in the extremity and precordial leads depressed or elevated S T segments and/or T wave inversions (fig 17) These changes accompany an anatomic substrate of *myocardial* fibrosis endocardial thickening and even ventricular aneurysm produced by the faulty *blood*

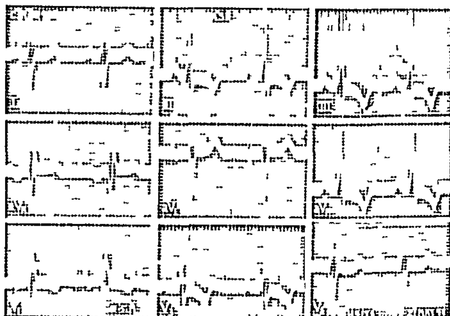


Fig 12 C R male 39 years Atrial septal defect bilateral thrombosis of the pulmonary arteries tuberculosis of the lung (necropsy) The broad and notched somewhat tall P wave diphasic in lead V_1 hints at a dilatation of both atria The deformation of the ventricular complex is compatible with right bundle branch block The coexistence of right ventricular hypertrophy cannot be excluded (Compare with morphologically similar QRS in a case of Eisenmenger's complex fig 14)

do not fail to appear in a good proportion of such cases [54] This naturally leads one to speculate on how much activation of the septum contributes to the form of the normal electrocardiogram Since the time of Monckeberg it has been known that in cases of a single ventricle the His bundle is kept intact* and that it lies on the posterior side of the ventricular wall Mahaim[55] has reported a remarkable case of trilocular heart with a single ventricle in which he could identify the sinoatrial and atrioventricular node with ease but was unable to find any continuation of the latter toward the ventricle or any His bundle However there was a muscular bridge on the posterior aspect of the heart between the left atrium and ventricle Despite the absence of the His system the electrocardiogram was not impressively changed the P R interval measured 0 16 sec, the QRS complex a little more than 0 10 sec and its form resembled a right bundle branch block

Electrocardiographic abnormalities reminiscent of those seen with myocardial infarction in the adult are encountered in infants and children

* This is explained by the embryologic asynchronism in the formation of the ventricular conductive system and of the interventricular septum

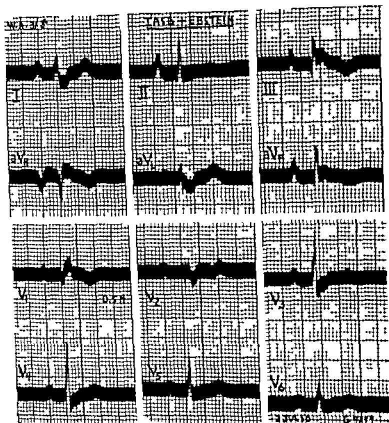


Fig 15 W A male 31 years Ebstein's malformation atrial septal defect (diagnosis from signs and cardiac catheterization) Features include P wave of increased voltage and duration (0 11 sec) a prolonged P R interval (0 23 sec) right deviation of the electrical axis of QRS with an increased duration (0 18 sec) and all the characteristics of right bundle branch block Low voltage of R wave in lead V_1 and V_2 with an abrupt increase in the size of this deflection in lead V_3 and the picture of right bundle branch block as seen in this figure have been described as typical of Ebstein's malformation [4, 20]

coarctation of the aorta ventricular septal defect, less often with atrial septal defect and pulmonary stenosis There is almost unanimous agreement that a high right ventricular pressure is absent in all such cases

Electrocardiograms obtained from the inside of heart chambers have a very special use In Ebstein's anomaly the tricuspid valve is displaced downward toward the apex thus a huge right atrium is produced the distal portion of which in reality corresponds with the inflow tract of the right ventricle This peculiarity lends itself to intracardiac exploration a catheter permitting registration of both pressure curves and the electrocardiogram



FIG 14 P B male 32 years Eisenmenger's complex (necropsy) The duration of QRS (0 11 sec) its configuration in lead V_1 (and V not reproduced) and the delayed onset of the intrinsicoid deflection (0 07 sec) in lead V_1 could be interpreted as incomplete right bundle branch block or right ventricular hypertrophy No substantial change in the form of the electrocardiogram occurred up to the time of the patient's death at the age of 37 years

supply to the myocardium In finding such changes, one must always be mindful of the fact that they may be brought about by any lesion affecting the coronary circulation of the infant be it inside the wall of the coronary artery (sclerosis) or outside of it (tumor, periarteritis nodosa) [47]

In discussing right ventricular hypertrophy, we have mentioned that in the right precordial leads due to the activation of the septum from right to left Q waves may occur which should not be confused with the necrosis effect of myocardial infarction The same warning applies to abnormal Q waves in the same areas, which according to Sodi Pallares Bisteni, and Herrmann [57] may be present in congenital and other cardiopathies if the right atrium is so large that the electrodes located in the right precordium face the epicardium of the right atrium instead of the right ventricle and register the potentials normally encountered on the surface or inside the right atrium If the right atrium is very large the Q waves may extend from position C_1 to C_6

An electrocardiogram absolutely within the accepted limits of normal is not rare in instances of congenital heart disease This can be accounted for by the preservation of normal morphology and dynamics or by the presence of abnormal forces counterbalancing each other A normal electrocardiogram is often found with patent ductus arteriosus aortic stenosis,

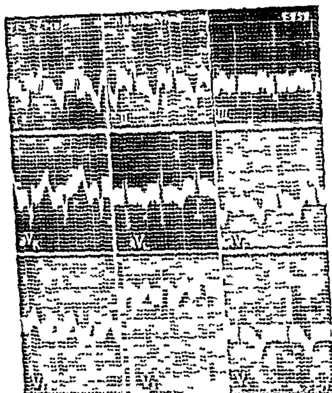


Fig 17 J F female [illegible] months Anomalous left coronary artery arising from the pulmonary artery endocardial fibrosis subendocardial necrosis (necropsy) The abnormally displaced S T segment and the abnormal T waves reminiscent of those seen in adults with impaired coronary circulation arouse suspicion of anomalous origin of one coronary artery (or both arteries) although no Q waves are present

the tricuspid valve Emslie Smith and associates[60] suggest the use of intracardiac tracings for the distinction between valvular and infundibular pulmonary stenosis the abrupt change in the form of the electrogram during withdrawal from the pulmonary artery into the right ventricle is diagnostic of the valvular site of obstruction even if the pressure tracing is not

Arrhythmias in Congenital Heart Disease

Arrhythmias are not common in individuals with malformed heart possibly because of their lower mean age Prolonged A V conduction time * manifested by a prolonged P R interval has been described as

* In accordance with custom we include among arrhythmias the prolongation of the atrioventricular conduction time although in the strict sense of the term this phenomenon does not disturb the rhythm

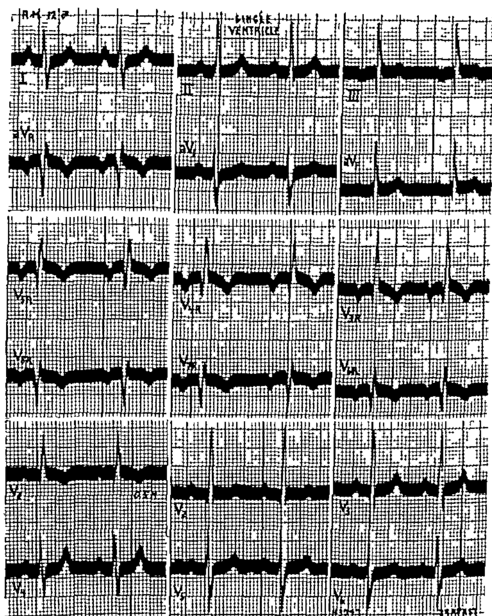


FIG 16 R M male 12 years Single ventricle pulmonary hypertension (diagnosis from signs angiocardiography and cardiac catheterization) Despite the absent interventricular septum the initial ventricular complex is of normal duration The electrocardiographic features are those of right ventricular hypertrophy

is introduced into the right atrium While the pressure curve reveals the location to be in the atrium, the presence of ventricular myocardium in the same cavity—diagnostic for this anomaly—can be demonstrated by either monophasic ventricular complexes[58] or ventricular extrasystoles[59] both provoked by slight pressure of the catheter against the septum just above

discussed and their significance evaluated Although in the overwhelming majority of cases of congenital heart disease the electrocardiogram is not specific for the malformation present its configuration may be a useful element in clinical diagnosis

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occurring with atrial and ventricular septal defects, Ebstein's malformation (fig 15), rarely in Fallot's trilogy and tetralogy, and coarctation of the aorta. Kjellberg[19] emphasizes the lack of its presence in patent ductus arteriosus, however, Cabrera[35] finds it in almost one fourth of cases with this anomaly.

Until recently, it has been believed that congenital complete heart block is indicative of a ventricular septal defect, but Campbell and Thorne[61] have conclusively shown how erroneous this assumption is. About one half of patients with congenital heart block have no associated anomaly. The characteristic features of congenital heart block are (1) a higher ventricular rate than in the acquired form, 40 to 70 in the former against 28 to 40 in the latter, (2) normal appearance of the ventricular complex.[61] In addition to interventricular septal defects, congenital complete A V block has been noted to occur with atrial septal defects, especially persistent ostium primum, Fallot's tetralogy, and coarctation of the aorta.[6, 63]

All the other forms of arrhythmia have no particular morphologic implication with the exception of atrial fibrillation which is seen in advanced forms of interatrial septal defect, especially among aged individuals,* in anomalous pulmonary venous drainage, in Ebstein's malformation,[64] and in decompensated patent ductus arteriosus.[44] When patients with congenital heart disease reach the stage of congestive failure they are apt to develop any kind of arrhythmia, extrasystoles being the most common.

According to Sodi Pallares and associates, anomalous atrioventricular excitation makes a not infrequent appearance in Ebstein's malformation, it has also been described in endocardial fibroelastosis. Ebstein's malformation is further characterized by a high incidence of frequent extrasystoles and by attacks of paroxysmal tachycardia.

Permanent or paroxysmal atrial flutter (usually acquired, very rarely inborn) and various forms of A V nodal rhythms and A V dissociation are met with from time to time, probably less often than in instances of heart disease of other origin. Paroxysmal tachycardia occurs in patients with anomalous atrioventricular excitation, and Miller[31] stresses its diagnostic importance in acyanotic infants with a large heart due to congenital rhabdomyoma.

SUMMARY

There has been presented in outline form an account of what recent advances in electrocardiography can contribute to the diagnosis of congenital heart disease. The electric changes which are encountered have been

* The oldest patients in our series of congenital heart disease were all women with interatrial septal defects and atrial fibrillation (age at death or last observation 66, 67, and 72 years, with onset of fibrillation at the age of 57, 61, and 70 respectively).

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14 Present Status of the Electrocardiogram in Myocardial Hypertrophy

CHARLES E KOSSMANN, M D

THERE ARE several aspects of the electrocardiogram in myocardial hypertrophy over and above those covered in Chapter 13 that should be discussed It is the purpose of this chapter to point out some inadequacies in the correlation between the electrocardiogram and hypertrophy of the heart and also to call attention to a somewhat more promising approach which involves attempts to relate the configuration of the electrocardiogram to the relative amounts of work that either or both ventricles must do

It is maintained by many that hypertrophy is an anatomic modification of the heart which is more evident from the electrocardiographic deviations it causes than from any other clinical or laboratory examination It is interesting that relative to cardiac hypertrophy the radiologist in general feels that the methods available to him are not as precise as the electrocardiographic method[1] Many papers have appeared that support the exact correlation between the electrocardiogram and the enlarged cardiac chambers which undoubtedly accounts for this point of view However there are some facts in these publications to be noted only on critical reading which make it obvious that the *method is accurate* in less than seven and probably in less *than five* out of every ten instances of hypertrophy

Two older autopsy series have been reported one of patients with right ventricular hypertrophy[2] and the other of patients with left ventricular hypertrophy[3] The disease in most of these patients was so far advanced that death resulted Even so using the best criteria available, both in extremity and in precordial leads the correctness of the diagnosis could be established definitely by the electrocardiographic method only in approximately 70 per cent of both series Clearly in less advanced stages of hypertrophy of either ventricle the incidence of positive electrocardiographic findings will be lower

More recently a paper on the electrocardiogram in left ventricular hypertrophy contained a statement that in 100 necropsies it was possible by using several investigators criteria to attain a 96 per cent accuracy in diagnosis[4] This statement when read quickly is impressive, but also misleading The authors pointed out that by selecting 100 cases of left ventricular hypertrophy proved at necropsy and then going back to the electrocardiograms to determine how accurately the diagnosis could be

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Cabrera and Monroy.[8] In their papers they point out that hypertrophy can occur not only as a result of an increase in the diastolic length of the myocardial fiber with an increase in tension up to a certain limit, as defined by the law of Patterson and Starling,[7] but also by an overload in systole. In the latter situation, exemplified by aortic stenosis, the left ventricular chamber may not be enlarged although the walls are thickened (concentric hypertrophy). On the basis of the two assumed origins of hypertrophy the concepts of systolic overload (increased resistance to outflow) and diastolic overload (increased initial fiber length from increased diastolic inflow) have been developed. The electrocardiographic abnormalities characteristic of each of the four possibilities for the two ventricles may be summarized as follows:

Ventricle	Overload	Electrocardiogram
Right	Diastolic	Classical right bundle branch block
	Systolic	Prominent R wave (or RS, Rs, qR) in lead V_1
Left	Diastolic	Large late R in leads V_5 and V_6 with upright high T wave (ventricular gradient normal direction, large magnitude)
	Systolic	S-T and T abnormal in left sided leads (ventricular gradient absent or diminished)

The overload concept is an interesting one but the degree of accuracy of the correlation between the hemodynamics and the electrocardiographic abnormalities requires further study. For example, the significance of minor degrees of intraventricular block as a cause of the electrocardiographic configuration of left ventricular systolic overload has not been fully appreciated (Chapter 10, fig. 26). Further, the percentage of clinical conditions with the necessary hemodynamic aberrations showing the required electrocardiographic abnormalities is considerably smaller in our experience than in the experience of Cabrera and Monroy (Chapter 13).

Cosby and his associates[8, 9] have made a correlation of the electrocardiogram with right ventricular work and ejection pressure in a variety of acquired and congenital defects. Right ventricular work was calculated as a product of the cardiac index and the gradient of the mean pressure between the right atrium and the pulmonary artery corrected for the specific gravity of blood.

Obvious differences were noted in the two groups. In congenital heart disease, characteristic changes in the electrocardiogram were noted with lower systolic ejection pressures (less than 30 mm. Hg) and with smaller

made by these criteria, they performed a study which lacked specificity. They could not deduce from their data how often the various criteria were met in normal subjects or, more important, in patients with disease of the heart other than hypertrophy. In addition, they did not know what percentage of cases with hypertrophy not severe enough to cause death was associated with a normal or an abnormal electrocardiogram. Lastly, the high correlative percentage was obtained only if one of multiple criteria was required to make the diagnosis. The criteria of almost all workers in the field include S T segment *depression and lowered or inverted T waves* in leads from the left side of the precordium or the left arm. Though not stated, it is suspected that this was the most frequent, singly met criterion in the study. The number of chemical, physiologic, pharmacologic, thermal and mechanical factors which can affect the final ventricular deflections of the electrocardiogram in this manner are legion, and certainly changes in the S T segment and T wave by themselves can hardly be taken as a criterion of anything anatomic. In the same study, as soon as two criteria were insisted upon the best percentage of correct diagnoses was 64 per cent.

If the correlation between *hypertrophy and the electrocardiogram is as* imperfect as intimated, it is even more so with other intrinsic lesions of the myocardium, a point which has been repeatedly stressed by electrocardiographers past and present.

Two interesting studies relative to right ventricular hypertrophy have been reported by Walker, Helm and Scott.[5] In the first of these studies the authors selected 22 cases which demonstrated hypertrophy of the right ventricle at necropsy. They then investigated the electrocardiographic file. Of the 22 records five displayed one of the electrocardiographic criteria established by Sokolow and Lyon[10] and three showed one criterion of Myers.[2] The remainder showed none of the usual graphic manifestations of right ventricular hypertrophy. Then these investigators selected 12 cases from the electrocardiographic file which showed evidence of right ventricular hypertrophy in the record. Of these 12 patients definite right ventricular hypertrophy had been demonstrated at necropsy in eight.

These studies demonstrate that the exactness of the correlation will depend somewhat on how the data are collected. Secondly, they indicate quite vividly that the electrocardiographic and anatomic correlation, at least in right ventricular hypertrophy, is far from perfect.

The Electrocardiogram and Circulatory Hemodynamics

A direct or indirect correlation of the electrocardiogram with work of one or the other chambers has been undertaken by several groups.

One of the interesting concepts resulting from such an approach is the one of systolic and diastolic "overloading" of the heart introduced by

PART IV RHYTHMS

15 Excitability of Cardiac Muscle and the Action of Antiarrhythmic Agents

MORRIS KLEINFELD, M.D.

THE PROPERTY of tissue or cells to respond to environmental changes is known as excitability. In the case of muscle, responsiveness to various stimuli results in contraction. Adrian, in 1920, introduced the modern approach for studying the excitability of the heart. With graded electrical stimuli above the threshold, he determined a strength-interval curve which demonstrated an absolute and relative refractory period.[1]

Hoff and Nahum (1938) were the first to relate the excitability cycle in the mammalian heart to the electrocardiogram. In their experiments, the hearts of dogs, cats, and chimpanzees were exposed and testing stimuli applied at random from a thyratron stimulator approximately 1 second apart. The relative refractory period was observed to occur on the descending limb of the T wave and was often followed by a period of supernormality before excitability returned to threshold levels.[2] Supernormality is a period in the excitability cycle when the tissue is responsive to subthreshold stimuli; when present, it occurs at the end of the refractory period of the *cardiac* cycle. The supernormality occurred in animals anaesthetized with barbiturates but was not observed in unanesthetized decerebrate preparations.

Wiggers and Wégria (1939) demonstrated the "vulnerable period" for eliciting multiple extrasystoles or fibrillation in the dog's heart by applying single D.C. shocks of 10 to 30 milliseconds duration to the dog's ventricle during the T wave.[3]

Segers, in 1942, obtained monophasic action potentials in the isolated perfused frog heart by means of a calomel half cell filled with saturated KCl and attached to the ventricle. He observed an association between supernormality and negative after potentials and subnormality with an enhanced positive electrical after potential (Chapter 1). He noted that extrasystolic arrhythmias were produced by those agents which augmented the negative after potential. Among these were increased Ca in perfusion fluid, aconitine, veratrine, epinephrine and digitalis glycosides. On the other hand, agents which were associated with a positive after potential such as acetylcholine, quinidine, cocaine hydrochloride and increased K resulted in a diminution of excitability and inhibition of spontaneous

amounts of right ventricular work (1 Kg m /min /M) than with mitral stenosis In the latter, on the other hand, electrocardiographic abnormalities were often absent if the systolic ejection occurred at a pressure range of 30 to 60 mm Hg but were usually present when the latter was above 60 mm Hg In addition, the work load had to be more than 1 Kg m /min /M for the electrocardiogram to reveal characteristic abnormalities

The studies would seem to indicate that increased ventricular work as calculated and elevated ventricular ejection pressure are not the only determinants of electrocardiographic abnormalities, at least so far as the right side of the heart is concerned

In summary, it may be stated that accuracy of making a diagnosis of hypertrophy from the electrocardiogram alone is a good deal less than is generally believed A correlation of the electrocardiogram with the contractile cardiodynamics is a relatively new approach to the problem which *shows evidence of considerable promise*

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activity[4] Microelectrode techniques have not verified Segers work Weidmann found no such correlation in cat papillary muscle although he obtained small negative after potentials with stretched papillary muscle preparations[5] Our own study[6] using isolated perfused frog heart, likewise did not disclose any consistency Barium, at times did cause a negative after potential but no associated supernormality

In the study of excitability the application of submaximal stimuli during the cardiac cycle usually elicits a period in which the heart is prone to fibrillation This is known as the vulnerable period Orias et al[7] in 1950 reported their studies on excitability in the dog heart and observed the phenomenon of the dip' a period of increased excitability observed during the relative refractory period Brooks et al[8] demonstrated that the latter dip coincided with the vulnerable period of Wiggers and Wégria This made it necessary to modify the classic view that excitability decreases smoothly during the relative refractory period Our own observations[9] as well as those of Lanzoni and Clark[10] have confirmed the presence of the dip in the turtle and dog heart

Technique for Studying Excitability

The technique introduced by Suckling et al[11] is the most accurate method available for studying cardiac excitability A similar procedure is used in our laboratory A plastic disc containing four stimulating electrodes is sutured to the base of the heart two electrodes serve as anodes and the other two as cathodes for the driving and the test stimuli The ventricle is driven between 40 to 60 beats per minute from a square wave stimulator with a pulse of 2 milliseconds duration delivered through an isolation transformer This stimulator also triggers a second stimulator to provide a square wave test stimulus of calibrated delay strength and duration The stimulus is usually inserted at every tenth beat The current in milliamperes is calculated from the voltage drop (measured on an oscilloscope) across a 100 ohm resistor in the anode side of the test level A monopolar ventricular electrogram observed on an oscilloscope indicates the various positions along the heart cycle where the stimulus is inserted The instrumentation is schematically illustrated in figure 1

Excitability studies can be performed either during diastole or systole When studied during diastole the plotting of the results on a graph gives a *strength-duration curve* which is usually a smooth curve as illustrated in figure 2 The strength duration curves vary with heart rate and the thresholds are higher for the ventricle than for the atrium Studies carried out in systole are more fruitful for an understanding of the threshold properties of cardiac muscle The duration of the rectangular pulse is constant for each study while the strength and cycle interval are varied When the

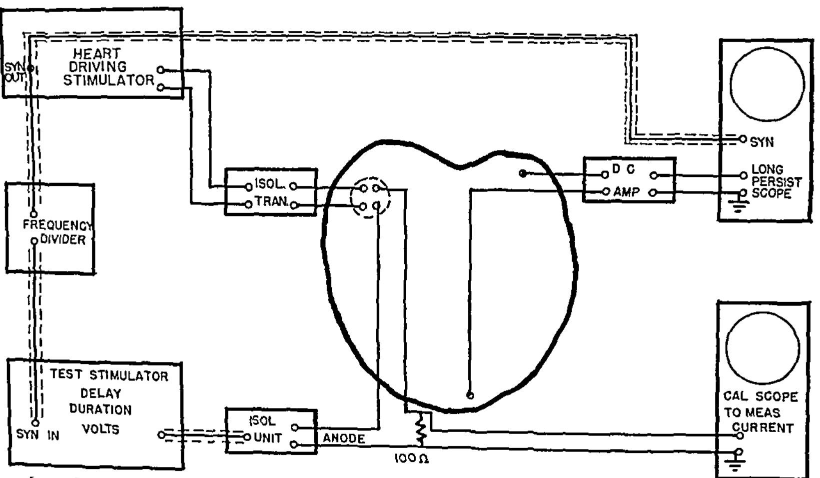


Fig. 1 Schematic diagram of the stimulating and recording circuits used to determine the excitability of cardiac muscle

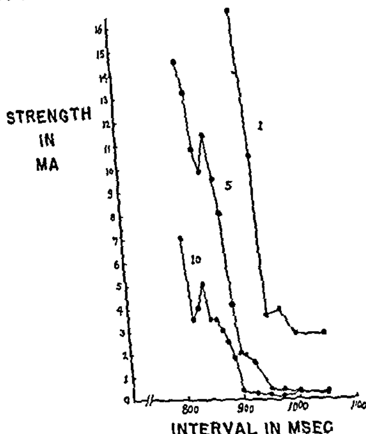


Fig Strength interval curves of turtle ventricle showing the time course of re[co]very of excitability as determined by stimuli of 1, 5 and 10 m[s]ec duration

of these tran[s]ient periods of enhanced excitability to stimuli applied during the relative refractory *period* There is no evidence that they are associated with any oscillatory changes in membrane *potential* of cardiac muscle The dip phenomenon suggests *periods* of relative supernormality which can be related to the period of *vulnerability* observed by Wiggers and Wégria[2]

VARIABLES WHICH AFFECT EXCITABILITY OF CARDIAC MUSCLE

Heart Rate An increase in heart rate shortens the absolute and total refractory periods without a change in *duration* of the relative refractory period This is observed as a shift to the left in the strength interval curve In the atria and ventricles of dogs Siebens et al[13] observed that neither the dip nor the minimum dia*stolic threshold* nor rate of conduction of a propagated beat were altered at rates up to 250 to 300 beats per *minute*

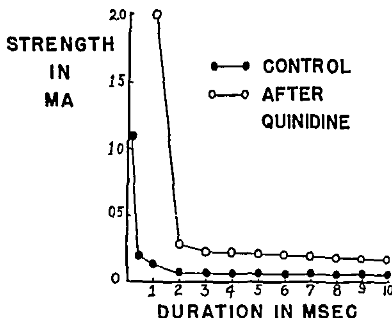


Fig 2 Strength duration curves of frog ventricle showing excitability in diastole prior to and after injection of quinidine sulfate (0.2 mg) into the aorta

results are plotted on a graph, the resulting *strength interval* curve will show an absolute refractory period followed by a relative refractory period. Furthermore as Orias et al originally showed a "dip" during the relative refractory period will usually be observed. Not infrequently two dips will be present an early one of short duration and a later major dip. A typical example of a strength interval curve is illustrated in figure 3. These curves also vary somewhat with the heart rate.

Strength interval curves yield information on the absolute and relative refractory periods, supernormality and the "dip" phenomenon. It is also possible to obtain information on latency of response to the test stimulus. The latency between the time of application of the test shock and the appearance of the propagated action potential is composed of a very short true latency and a longer conduction time. Using multiple electrodes, conduction time can be measured and the true latency estimated. Brooks et al[12] found that latencies of response vary greatly during the cardiac cycle of the dog. They observed that throughout diastole, when the level of excitability is constant the over all latency between test shock and propagated response is unchanged, whereas in the relative refractory period the latency is much longer and increases in length with increased refractoriness. Furthermore the latency between stimulus and response is most often changed when the effective test pulse is applied during the "dip" in the strength interval curve.

At present, there is no complete explanation of the underlying cause

ture the relative refractory period is slightly lengthened The differences observed between the temperature coefficients of the plateau and the final phase of repolarization of the transmembrane potential is in agreement with the different sensitivities of the absolute and relative refractory periods to cooling Conduction times and latencies of response are lengthened by cooling There is no change in amplitude or duration of the dips

In essence the slowed conduction and the minor changes in excitability the disproportionate changes in various cardiac tissue and the possibility of augmented temperature gradients in the heart may offer some explanation as to why both atrial and ventricular arrhythmias are prone to develop during cooling and rewarming

Drugs There are a number of agents known to enhance the vulnerability of the myocardium to the production of arrhythmias Major among these are the sympathomimetic and parasympathomimetic compounds Among others are

1 *Veratrum Alkaloids* Large doses are known to cause arrhythmias and even ventricular tachycardia and fibrillation [9] Matsuda [1] found that crude preparations produced a moderate prolongation of the total refractory period of the dog heart both the absolute and relative refractory period being prolonged Excitability was decreased and conduction particularly in the A V bundle was slowed

The effects on the transmembrane potential are (1) a prolongation of repolarization and (2) an increased tendency to spontaneous firing The time and degree of prolongation is proportional to the concentration of the drug The rhythm of spontaneous firing is somewhat irregular occurring at a time when repolarization of the preceding action potential is *almost* completed Hoffman et al [12] showed that spontaneous activity appeared in runs lasting from a few seconds to several minutes Species difference were observed with rats being more sensitive than dogs A combination of slowed conduction and an imbalance of effects on the excitability and refractoriness was *postulated to* explain the increased vulnerability of the heart following administration of these drugs

2 *Chloroform* The production of ventricular fibrillation in animals under light chloroform anaesthesia by *injection* of epinephrine is well known Acierno and DiPalma[29] and others have shown that chloroform depresses excitability but shortens the refractory period Others have found that this agent in small doses increases excitability but larger doses depress excitability [12] Hoffman et al [22] postulated that the combined depressant and excitant action initiated by the drug in situations during which the vagi and sympathetic nerves are also brought into action may be responsible for the occurrence of fibrillation

3 *Cardiac Glycosides* The cardiac glycosides in high concentrations

Vagal Stimulation and Acetylcholine Vagal stimulation and acetylcholine increase the conduction velocity of a propagated response in resting atrial muscle Brooks et al[12] have noted a distinct effect of both on the atrium in the absence of any significant effect on the excitability of the ventricle in the dog They demonstrated that vagal activity and acetylcholine greatly enhance the vulnerability of the atria to flutter and fibrillation[1] J H Burn et al[14] have induced atrial fibrillation in the heart lung preparation of the dog by slow infusion of acetylcholine and the application of electrical stimulation to the atria The fibrillation could be maintained indefinitely after the electrical stimulus ceased by continuing infusion of the drug

Chemical Mediators Stimulation of the cardiac sympathetic nerves in dogs produces only slight alterations in duration of the total refractory period of the ventricle and atrium Both an increased and decreased interval of the cycle length have been observed The sympathomimetic amines such as epinephrine and norepinephrine produce considerable increases in heart rate, in conduction velocity in the atrium, A V tissues and ventricle and a moderate shortening of the total refractory period[15]

Temperature Two factors appear to be important in thermal influences on the heart These are the rapidity of temperature change and the production of a temperature gradient within the heart created either by heating or cooling a part of the organ

Localized heating and cooling may produce arrhythmias and actual fibrillation Heating of any portion of the myocardium accelerates processes occurring at the site so that ectopic beats may originate in the area[16] Cooling is more likely to establish a potential gradient capable of creating an ectopic focus of beat origin as has been shown by Scherf et al[17] Localized cooling has been shown to produce a current of injury between normal and cooled areas and to slow conduction in the latter thus providing an opportunity for re entry

Generalized cooling may cause heart stoppage at temperatures of approximately 13°C in mammalian hearts (dog) Spontaneous arrhythmias are a common consequence of such cooling Hegnauer and Covino[18] observed a metabolic acidosis at low temperatures and this may affect the responses of the heart but the rate of pH change in the determination of cardiac excitability and vulnerability to fibrillation has not been ascertained

The effect of temperature on diastolic thresholds for the production of extrasystoles of the dog heart is not consistent according to the observations of Pinkston et al[19] The refractory period is profoundly affected by cooling and leads to a lengthening of the total refractory period of the ventricle almost entirely in the absolute phase At extremes of tempera

eters was significantly less than that of quinidine sulfate and procaine amide Latency was increased only when relatively high doses were administered

Inorganic Ions

Calcium has been reported to be a stabilizer of the membrane since it has been found that high calcium decreases the sensitivity of the heart to applied stimuli Weidmann[25] has demonstrated that this is due to an elevation of threshold which makes necessary a stronger stimulus for producing an action potential Low calcium has an opposite effect

Sodium within a range compatible with life in the intact animal has little direct effect on the excitability of the heart muscle although in experiments on the isolated heart when severely depleted sodium was replaced by choline chloride to maintain the osmotic pressure Clark[6] found a complete loss of excitability

Small changes in the level of *potassium ions* have profound effects on the excitability of heart muscle An increase in potassium results in a decrease in excitability while the reverse occurs with a decrease in potassium

Barium chloride has not shown a consistent effect In the isolated cat papillary muscle using 0 28 to 2 8 mM barium chloride the threshold of excitability in some instances was lowered and in others raised In five out of seven muscles Greiner and Garb[7] observed that an automatic rhythm supervened

Antiarrhythmic Agents

Techniques Employed

A number of methods exist for studying antiarrhythmic agents Intact hearts isolated perfused hearts and strips are employed Not infrequently a heart lung preparation is preferred For rapid screening of new drugs isolation techniques have been found of value especially for a comparison of the pharmacologic activity of drugs The procedures employing intact hearts are preferred however because they represent a more normal physiologic environment for the heart Arrhythmias can be induced by such means as (1) electrical shocks (cathodal anodal or bipolar) (2) coronary artery ligation (3) electrolytes (calcium in rat) and (4) drugs In dogs under benzol chloroform or cyclopropane anaesthesia the administration of small doses of epinephrine consistently produces ventricular fibrillation Anticholinesterase agents such as *tetraethyl pyrophosphate* followed by electrical stimulation and acetylcholine have been employed to produce atrial fibrillation[28] The antiarrhythmic drug to be evaluated is usually administered prior to induction of the arrhythmia

enhance repolarization, thus shortening the duration of the membrane action potential Some of the other drugs which have the ability to increase vulnerability do the same These drugs have been found to shorten the refractory period of both the atrium and ventricle of the dog's heart and to slow A V conduction [4]

4 *Reserpine* This agent lengthened both the absolute and relative refractory period and raised the diastolic threshold This is illustrated in figure 4 In equivalent dosages the effect of reserpine on these param

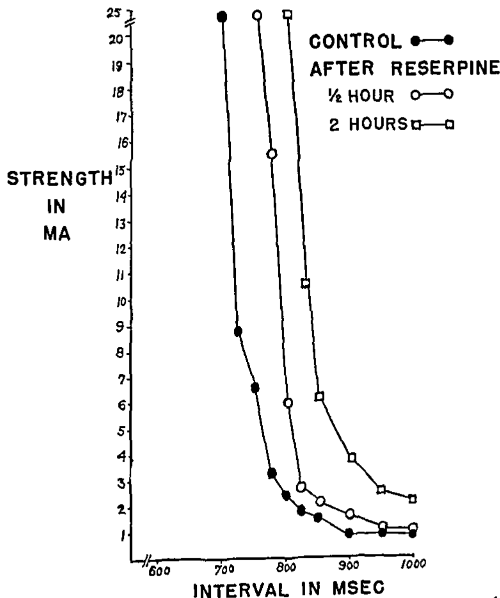


FIG 4 Effect of reserpine (0 5 mg /Kg) given intravenously on the excitability of the ventricle of the intact turtle heart

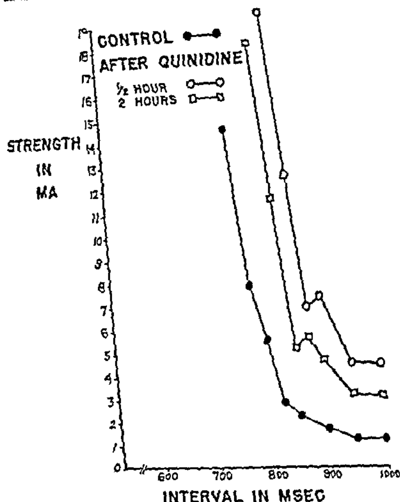


Fig 5 Effect of quinidine sulfate (0 2 mg/kg) given intravenously on the excitability of the ventricle of an intact *turtle heart*

and only to a lesser extent the relative refractory *period* It did not change the diastolic electrical threshold nor conduction time in the ventricle of the dog It was effective in suppressing experimentally induced ventricular tachycardia

A review of the data of the effect of the various agents on cardiac excitability discloses that no single parameter is uniformly related to the production of vulnerability to multiple firing or fibrillation This is best illustrated in Table I in which a number of agents that under varying conditions are known to enhance vulnerability are shown and their effects on the various parameters of excitability given.

The Effect of Antiarrhythmic Agents on the Excitability of the Heart

A number of antiarrhythmic agents have been evaluated in terms of their effect on the following parameters (a) absolute refractory period, (b) relative refractory period, (c) diastolic threshold, (d) conduction velocity These studies have been performed on intact hearts, and on muscle strips or bundles

Quinidine

1 Atrial Excitability Quinidine slows the rate and prolongs the relative refractory period of the atrium of the dog It has been suggested that it is this property which makes quinidine effective against atrial fibrillation Although the threshold is elevated the "dip" in the strength interval curve is not abolished and is maintained at the same relative position in the relative refractory period Intraventricular conduction velocity is slowed [1]

2 Ventricular Excitability Similar changes were observed by Woske et al [9] in the ventricle The average increase in diastolic thresholds was *greater in the ventricle than in the atrium Although there was an elevation* in diastolic threshold and a decrease in vulnerability fibrillation was not often abolished by the doses employed whereas quinidine did abolish fibrillation in the atrium resulting from suprathreshold test pulses Figure 5 shows the effect of quinidine sulfate[6] on the strength interval curve in the turtle heart

Procaine Amide

1 Atrial Excitability Intravenous infusion of procaine amide in doses of 30 to 40 mg/Kg increases the total refractory period in the dog's atrium *the relative more than the absolute refractory period The diastolic thresh*old is somewhat elevated The general configuration of the strength interval curve shows an elevation in thresholds but a similar shape to the control curve The dip is not consistently altered Conduction is slowed particularly in A V conductivity [9]

2 Ventricular Excitability Procaine amide increases the absolute and relative refractory periods only slightly The threshold of resting excitability in the ventricle was shown by Woske et al [29] to increase more markedly than that of the atrium with similar concentrations of the drug This may explain the greater effectiveness of the drug in ventricular arrhythmias These same authors found a striking change in vulnerability in the absence of any appreciable alteration in the duration of refractoriness Figure 6 shows the effect of procaine amide on the strength interval curve of the turtle heart

Amboneslyl

Lanzoni and Clark[10] have shown that in doses of 40 mg/Kg administered intravenously, this drug affected chiefly the absolute refractory period,

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V_F, II and III P invisible i e merged in QRS an inverted P wave following QRS in leads V_F, II and III The last type is the least common *

The AVN in man is a structure about 5 by 3 by 2 mm located on the right side of the interatrial septum somewhat to the left of the coronary sinu Its seat so inacce ible in experimental work, reminds one of the pituitary gland in the skull And if the simile may be extended a little further these two structures can also be compared in of ir as their im portance is concerned the former being the coordinator of the rhythmic activity of the heart the later the mo t important single endocrine organ of the whole endocrine system

The simplest manifestation of independent nodal activity is an A V *nodal extrasystole* which is premature relative to the expected beat Its main characteristic is the change in the time relation of the atrial to the ventricular complex the P R interval may be shortened to le s than 0 12 sec , the P wave may be buried in the QRS complex or may follow it The P wave may be negative or positive although its inver ion in the leads mentioned above represents the clinically accepted form The QRS of an A V nodal extrasystole is often slightly aberrant the similarity of the abberrance to that of right bundle branch block has been emphasized by Katz and Pick [4]

In A V nodal extrasystoles with an R P sequence the limit of the R P interval uncomplicated by a conduction defect is et at 0 20 sec In the majority of cases the pause following an A V nodal premature contraction is not compensatory Exceptionally an A V nodal extrasystole may be interpolated between two SAN beats, this combination, of course pre supposes a block in the retrograde conduction of the extrasystolic impulse through the atria to the SAN

If A V nodal extrasystoles follow each other at a rapid rate (the range is wide 100 to 270 per minute) an A V *nodal tachycardia* ensues The rhythm is rather regular especially with higher rates Katz and Pick[4] make a subtle distinction between A V *nodal tachycardia* and A V *nodal paroxysmal tachycardia* the rate of the former being 60 to 100 and that of the latter above this level However they admit the distinction is somewhat arbitrary and empha ize the clinical features of the paroxysm as the most important criterion for differential diagno is The attack of tachycardia may be hort (a few seconds or minutes) or it may last hours

* Our experiments in dogs have shown that a definite A V nodal rhythm may be present while a positive P wave is inscribed in all the bipolar extremity leads either preceding the ventricular complex at a shortene l or normal distance or following it That the e or similar forms oc ur in man has been suggested by several authors and in reality some clinical tracings clo ely resemble the electrocardiograms obtained in our experiments with the SAN totally eliminated (see experimental ob ervations below and reference 3)

16 The Sinoatrial Node, the Atrioventricular Node, and Atrial Dysrhythmias

JOSEPH V BRUMLÍK, M D

ATRIOVENTRICULAR NODAL ACTIVITY occurs spontaneously or can be produced experimentally in the human or in the animal heart either by suppressing the predominant rhythm of the sinoatrial node (SAN) or by enhancing the automaticity of the atrioventricular node (AVN) Such activity may be transitory or permanent

Clinically, the temporary forms are more common by far than the permanent ones Of the great number of patients seen and electrocardiograms studied since 1920, only three instances of A V nodal rhythm have been encountered that were of more or less permanent form, i e, of several years' duration

A V nodal activity can invariably be induced in healthy subjects by an intravenous injection of a sympathomimetic drug e g neosynephrine[1,2] In patients with prolonged A V conduction due to rheumatic activity A V nodal rhythms can be provoked by the patient holding his breath or other maneuvers[3] They are regularly registered during thoracic operations after the chest has been opened[4] Some forms of A V nodal dominance occur with various diseases of which none is specific Other forms merge so easily out of and into the sinus rhythm that they cannot be recognized without the aid of electrocardiography and are considered by some to be a variant of the normal

At the outset it should be stated that the commonly accepted nomenclature of A V nodal rhythms will be adhered to without entering into a discussion of whether all forms which are ascribed to AVN activity really originate in the AVN * No one has yet demonstrated their origin to be in this structure, but from the appearance of the atrial waves and the time relation of these waves *to the ventricular complex, it is reasonable to assume that the impulses arise there There is also an anatomic justification* for this assumption the microscopic similarity of the two nodes and the geographic location of the AVN A V nodal arrhythmias deeply influenced by the functioning or nonfunctioning of the SAN, may occur in a variety of clinical forms such as extrasystoles tachycardia, escape or as an autonomous rhythm

Any of these arrhythmias will show one of the following basic electrocardiographic types a shortened P R interval with P wave inverted in leads

* *It has been stressed that it is* sometimes impossible to distinguish between low atrial and A V nodal beats[5]

AVN whereby the atria are activated from above and below until the excitation waves meet and cancel each other. The idea of synchronous activity of two foci would be in conflict, of course, with the concept* of only one pacemaker being in control at any given time, a concept to which we subscribe. Additionally, there are other objections against the case of fusion beats in this instance. First, the proof of two simultaneous impulses spreading in opposite directions in the atria has not been advanced; second, if the form of the P wave originating in the SAN is plotted against the negative P wave produced by an impulse proceeding backward from the AVN, the resulting curve does not resemble the so-called transitional complexes; third, the chance of there being an identical discharge rate of any two physiologic impulse-generating centers over even a short period of time is exceedingly small*; fourth, complexes identical in shape with the mentioned transitional complexes are obtained experimentally in hearts completely deprived of the SAN with the pacemaker in the AVN only. For all these reasons we think that in the "wandering pacemaker" the pacemaker oscillates between SAN and AVN, i.e., jumps from one center to the other. Of course, to accept the validity of this concept, we have to admit that an impulse may originate in the AVN and yet be represented by a positive though abnormal wave in the extremity leads, an idea defended by Scherf and Shookhoff[9] many years ago and again confirmed in recent experimental work.[10,11]

No useful purpose seems to be served by *retaining* the old nomenclature of upper, middle, and lower forms of AVN activity based on the time relation of the P wave to the ventricular complex (in front of, simultaneous with, and following QRS), because there is no real proof of a distinct location in the node of the origin of the respective impulses. This nomenclature was introduced by Zahn[12,13] in 1912 and 1913, who reported that by introducing an endoscope into a dog's beating heart he could visualize the AVN, differentiate its upper, middle, and lower region, and by warming each part separately (after destruction of the SAN) obtain characteristic tracings,† i.e., the atria contracting ahead of, simultaneously with, or following the ventricles. It is not clear how he was able to discern so tiny a structure as the AVN and how, moreover, he was able to localize the thermode exactly in three distinct parts of it by means of his endoscope in a heart which was beating and was filled with blood. The AVN cannot

* This objection is not valid if Grant's[2] theory about the subordination of the AVN rhythm to that of the SAN rhythm is correct, because two identical rhythms would be present even in normal sinus rhythm; nevertheless, both rhythms are dominated by the rate of just one focus, i.e., the SAN.

† Zahn registered the contractions of atria and ventricles *separately* by means of suspension curves.

days, or weeks Instances of A V nodal tachycardia representing a permanent rhythm are also known[7]

The A V nodal extrasystole must not be confused with A V *nodal escape*, which is considered to be a manifestation of an inherent automatism of the AVN coming into play when the impulse from the SAN fails to arrive The A-V nodal escape, therefore, is characterized by a longer than normal pause preceding an A V nodal complex of any of the types already mentioned If there is a sinus arrhythmia present in such a case—and there usually is—auscultation of the heart does not permit differentiation of the nodal beat from a sinus contraction following a longer diastolic pause A V nodal escape is, as a rule preceded by a sinus beat, but exceptionally it follows a post extrasystolic pause It is usually *single but may occur* in groups If there is more than one nodal escape it must be assumed that the activity of the SAN has stopped or that the impulse formed therein has been prevented from reaching the atrial myocardium (*sinus standstill, sinoatrial block* or *dissociation*)

If there are more than three nodal escapes in succession, we usually classify the group as *A V nodal rhythm* The autonomous rate of the latter *is between 50 and 88 per minute, more often on the slower side* As a transitory phenomenon it is not uncommon, the permanent form which is extremely rare implies a lower rate of the SAN, its destruction or a sinoatrial block Electrocardiographically, all three basic A V nodal configurations may occur At higher rates the rhythm is rather regular with the slower ones, it fluctuates substantially It cannot be distinguished from a rhythm originating in the undivided common bundle (stem) *If combined with a bundle branch block the picture is identical with* that of an idioventricular rhythm

Rather frequently, one of the classic nodal forms makes its appearance periodically as a rule, during a slowing of the basic sinus rhythm The typical nodal complexes are preceded and followed by a few beats displaying a shortened P R interval and deformed P waves Such a sequence in rhythm, apparent conduction time, and form of the P wave is described as a *"wandering pacemaker"* (i e from SAN to AVN) *The term might* make one think that the pacemaker moves from the SAN to the AVN (and vice versa) through the atrial myocardium and that "en route" it emits impulses which account for the abnormal P waves and shortened P R intervals However, a systematic traveling of the pacemaker through the atrial myocardium devoid of a conductive system is unimaginable The explanation of these "transitional P summits"[8] is rather difficult if we reject the shift of the *impulse generating focus through the atrial* muscle They are attributed by some authors to so called fusion beats that is, to a simultaneous discharge of impulses both from the SAN and

the present time) It is felt that this is a parasystolic rhythm produced by the coexistence of two foci both generating impulses one at a slower rate in the SAN the other at a slightly higher rate in the AVN or any part of the junctional tissue above the bifurcation The AVN dominates the ventricular the SAN the atrial rate In order that this may happen, a blocking of the retrograde conduction of impulses from the AVN (or His-bundle) has to be postulated However conduction from the atria to the ventricles is possible, and it takes place when the SAN impulse reaches the ventricles just at the end of the refractory period before the AVN impulse has been formed Then the SAN impulse activates not only the atria but the ventricles also (so called interference or capture) The postulated condition of the AVN or its vicinity that permits conduction from the atria to the ventricles but not vice versa is termed unidirectional block Clinically this arrhythmia occurs almost exclusively as a result of digitalis (and especially digitoxin) toxicity The correct diagnosis is often missed because the tracing resembles a tachycardia interrupted by extrasystoles

According to Langendorf and Pick[25] an impulse may originate in the AVN and be conducted to the AV junction but not to the chambers Its path is not visible in the electrocardiogram but is manifested by the effect on the generation or conduction of the next supraventricular impulse This phenomenon is called *concealed conduction of an AV impulse*[2] and though highly theoretical the concept has proved advantageous in the explanation of various arrhythmias

Fusion beats in the atria have already been mentioned The term is applied to deformed P waves ascribed to atrial activation proceeding from two pacemakers one in the SAN and the other in the AVN But similar P waves can occur with just one focus (the AVN) functioning and are probably due to variations in conduction in the atrial myocardium

A dysrhythmia which involves the AVN and merits special consideration is represented by an electrocardiogram in which as a rule at a slower rate the P wave (positive or negative throughout or changing from one form to the other) moves around the initial ventricular complex (fig 1) The French call it flottement or chevauchement de P which means that the P wave is floating around the QRS complex or riding over it and leaning from side to side This is a good and vivid description of the behavior of the P wave This dysrhythmia is usually classified as a form of dissociation (dissociation isorythmique of the French authors) the idea being that the atria are activated by the SAN and that the ventricles are governed by a focus in the AVN or in the His bundle The stumbling block to this explanation lies in the identical rhythm of the two supposed foci As mentioned in another connection above such a rhythmic equality of any

be made out clearly even if, after the heart is stopped, the atria are opened wide and all blood is removed Nevertheless, Zahn obtained all three basic, and later commonly recognized, types of A V nodal activity The fact that the first type, characterized by a shortened A V interval, may be obtained by the stimulation of low atrial regions and that the last type, identified by ventricular activation preceding the atrial can be elicited from the undivided His bundle may explain Zahn's observations, and time has shown that nothing is lost if the obsolete nomenclature is abandoned

The inverted P wave in leads V_F, II and III, of A V nodal rhythms, irrespective of whether it precedes or follows the initial ventricular complex, represents retrograde activation of the atria The mean axis of such atrial waves is deviated to the left from the normal in the frontal plane, its angle alpha being −60° to −80° instead of the usual +50° to +60 The failure of the mean axis of the inverted P wave to point in the opposite *direction to the normal* (*which would correspond to an angle alpha of −120°* to −130°) indicates that the order of retrograde excitation of the atria is not the simple reversal of the sequence of atrial activation in sinus rhythm *described by* Lewis, Meakins, *and* White[8] *and by others* [16–19]

A special form of A V nodal activity although not so recognized by all authors is the so called *coronary sinus or coronary nodal rhythm* This form is characterized by a normal P wave upright in the bipolar limb leads and a normal QRS complex but with a P R interval shorter than 0 11 sec According to Katz and his school,[6,20] the impulse for such a beat arises in the part of the AVN around the mouth of the coronary sinus nearest the tail of the sinus node,' and spreads through the atria in a manner similar to that of the regular SAN beat, with a resulting normal (or near normal) P wave The curtailed P R interval is explained as in other types of AVN activity by the proximity of the locus of origin to the ventricles Scherf and Harris[21] deny the nodal origin of this form and consider it to be initiated in the SAN If a positive P wave is compatible with a pacemaker located in the AVN we see no reason why it could not be associated with a shortened P R interval, as seen in A V nodal rhythms with a negative P wave

Scherf and Schott[22] reserve the term coronary sinus rhythm (and extrasystole) to that form of A V nodal activity characterized by an inverted P wave in leads II and III and a *normal* duration of the P R interval An identical electrocardiographic configuration is of course produced by an AVN impulse with delayed conduction to the ventricles

An interesting though not too common, arrhythmia in which the A V nodal rhythm is the stronger element is the *dissociation with interference* (*originally* described by Mobitz[23] under the name of Interference Dissociation," a term later changed by Scherf[24] to the nomenclature used at

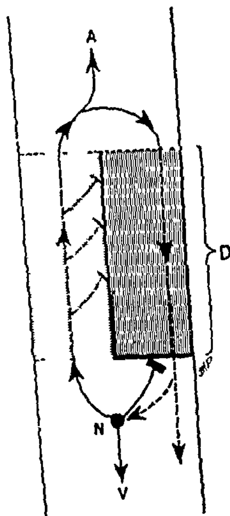


Fig 2 Katz and Pick's* diagram *explaining the* mech ani m of the reciprocal rhythm and the re entry phenomenon An impul e *originating* in or near the A V nodal tis ue (N) or arising elsewhere and *penetrating* it is conducted both to the ventri l (V) and through a pathway probably lo ated in the His *bundle* or the A V node (D) to the atria (A) On its way to the *atria* the impulse is blocke l in one *section* which is refractory for stimuli *arriving* from lower centers or from other part of the pathway it elf (darkly shade l right *half of the* rectangle D) but can pro ee l through oth r sections of the pathway (ligh ter shade l left half of the rectangle) To this type of di parate state of excitability in a small *area of the* con luc tive s t m Sch rf ha *given the* name functional *longitu linal* di ociation The sect n which has hown r fractorine s for retrograd impul *es is able* to con luct stimuli in an anterograde fa hion (unidirectional block) *Thus* one and the same impul e can re enter the functional ti sue an l activat the ventricl s again if it reache th m at a mom*ent* when they have become excitab*le* *The* cycle may be repetitive (ee fig 3 and 4) (From Katz and Pick *Clinical Electrocardiography* *)



Fig 1 Isorhythmic dissociation (flottement de P) The rhythm is slow (50 per min) irregular and identical in rate for atria and ventricles The salient feature *is the unfailing presence of the P wave in the vicinity of every QRS complex and the* oscillation of the atrial wave around the initial ventricular deflection (within the limits of ±0 24 sec) The atrial waves are positive in leads I and II diphasic (+ −) and slightly varying in shape in lead III (not shown) The angle alpha of the mean axis of the P wave is +30 which is somewhat to the left of the usual normal Similar tracings are usually interpreted as instances of a dissociation between the SAN and the lower pacemakers (in the atria the AVN or His bundle) Since we have seen analogous tracings in *experiments on canine hearts deprived of the SAN* such electrocardiograms are probably examples of an irregular A V nodal rhythm with varying conduction to the atria and ventricles and sinoatrial block The lack of negativity of the P wave is no objection to this concept (see text)

two autonomous physiologic foci is difficult to imagine Also, it is unnecessary as an explanation of the arrhythmia if we admit that a positive P wave in leads V_F II and III whether preceding or following the QRS complex, is compatible with an AVN rhythm We have good reason to believe that this is so After complete elimination of the SAN in animal when the AVN became the sole active pacemaker governing the heart we found not only positive P waves in the mentioned leads but also tracings analogous to those just discussed Others have noted the same thing [10, 11, 6, 27]

An AVN impulse transmitted both to the ventricles and atria can be reconducted through the junctional system to the ventricles If the impulse is premature, it gives rise to a so called *reciprocal extrasystole* In order that it can materialize, several theoretical conditions have to be anticipated These are best illustrated by Pick s and Langendorf s diagram [5] modified by Katz and Pick[6] (fig 2) which represents the state of the A V junction imagined to be necessary for establishment of the re entry phenomenon The basic idea of the concept of re entry of excitation is the vertical division (longitudinal dissociation) [9] of the junctional tissues into two paths one that conducts impulses arriving from a lower center in a retrograde fashion at the usual speed to the atria and another which picks up the impulse once it reaches the atria and reconducts it to the ventricles in an anterograde direction at a slower speed This latter line does not respond to



Fig 4 Reciprocal rhythm Same subject as in fig 3 A atrium A V junctional conducting tissues V ventricles Numerals between the vertical lines represent the atrial and ventricular cycle lengths respectively in hundredths of second The arrows indicate the direction of activation Upper electrocardiogram (lead II) starts with the same rhythm as shown in fig 3 It terminates with inscription of a P wave different from the preceding ones and is followed by a pause of 1 21 sec Cardiac activity recommences with an impulse originating in or near the SAN which is transmitted to the ventricles in 0 19 sec and evidently is conducted in a retrograde fashion *to the atria in 0 18 sec* After an interval of 1 14 sec another sinoatrial (or superior atrial) beat makes its appearance and initiates a sequence of *ventricular* and atrial complexes identical with the patient's habitual rhythm (fig 3) *except that the rate is higher* in the present record (146 per min) The records and the diagram illustrate the significance of the *inverted P waves They* mirror the retrograde conduction to the atria of an impulse which originally began in or about the SAN or elsewhere in the atria and proceeded normally to the ventricle During or after the ventricular activation the impulse *re-entered the A V nodal* tissue and the atria and the cycle began again The mechanism of a reciprocal rhythm presupposes a reduced speed in conduct*ion both to* the atria and to the ventricles and explains the prolonged R P and P R *intervals* Lower electrocardiogram is of the same patient same day The bipolar extremity leads show a sinoatrial rhythm induced with quinidine The pauses shown in *the upper* electrocardiogram also were produced by this drug (Electrocardiograms kindly provided by Dr *Bertha Rader*)

As a result of the loss of the governing pacemaker the AVN became dominant and activated the heart at a regular rate slightly slower than the usual sinus rhythm Either spontaneously or as a result of application of epinephrine (to which the AVN is known to possess a special sensitivity) all kinds of dysrhythmias commonly ascribed to the activity of the AVN developed but in addition various rhythms appeared which when encountered clinically have been attributed to an interplay of the SAN and AVN We do not wish to imply that a rivalry of the two foci cannot exist but in many instances the activity of the AVN alone suffices to explain seemingly complicated rhythmic disturbances mentioned in previous paragraphs

One part of our experiments was arranged to investigate the manner in

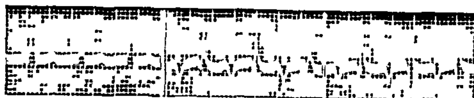


FIG 3 Reciprocal rhythm The record was obtained in a male aged 27 with no complaints and an otherwise normal heart It was the habitual rhythm in this subject and was known to be present at the age of 12 years (Electrocardiograms kindly provided by Dr Bertha Rader) The P waves which are isoelectric in lead I and inverted in leads II and III (followed by a positive atrial T deflection) point upward in the frontal and anteriorly in the horizontal plane (not reproduced) This indicates an A V nodal source of their origin The midposition of the P waves between the ventricular complexes makes it difficult to decide whether the impulse to which the atria are responding precedes or follows QRS The R P intervals measure 0 24 to 0 25 sec the P R intervals 0 20 to 0 23 sec both unusually long for an uncomplicated A V nodal rhythm

impulses arriving from below (unidirectional block) The impulse re entering the junctional tissue and the ventricles from above often disturbs the formation of the impulses in the junctional tissue so that the pause following a reciprocal beat is not compensatory The re entry (or echo) phenomenon may repeat itself several times (figs 3 and 4)

EXPERIMENTAL OBSERVATIONS

In the preceding discussion our experimental work on dogs has been mentioned several times * A few tracings registered in these experiments will be reproduced that may justify some of the points of view advanced All the experiments were carried out in dogs in which the SAN was surgically extirpated, together with a substantial part of the adjacent atrium The dogs were either sacrificed at the end of the experiment or in a minor series, permitted to live following an aseptic operation The latter group tolerated the operation well The animals without the SAN apparently behaved normally when the wound healed, a fact previously noted by Eyster and Meek[30] and by Jourdan and his group [6, 7]†

*This investigation was carried out by the author at the National Institute of Cardiology in Mexico City and was supported in part by a grant from the American Heart Association and in part by a grant from the Mercer County Heart Association Details of the technique used will be found in the original paper [13] The reproduced tracings (simultaneous direct leads from various points of the atrial surface and the endocardial lining of the interatrial septum together with a standard monitor lead) were taken by means of the Grass Encephalograph Model III

†In contrast to our predecessors our procedure consisted in a far more radical removal of the SAN and the tissue surrounding it In order to assure a complete elimination of the normal pacemaker *half of the right atrial wall a substantial* part of the superior vena cava was resected and the edges of the remaining tissue were sewn together

P wave in leads II and III sometimes appears if during the ensuing AVN rhythm of the commonest type (i e , simultaneous excitation of the atria and ventricle) a small amount of epinephrine is injected into the atrial musculature in the region of the AVN Figure 9 is an example of the phenomenon The form of the P wave in lead II does not substantially differ from that of a normal P wave however, the sequence of activation in the atria is at great variance with the normal pattern The tip of the left appendage (in sinus rhythm the last point to be activated) is depolarized far earlier than the right atrium which instead of *being the first* now is the last in the order of excitation close to or coinciding with the termination of the reference P wave

There is good reason to believe that these positive P waves have been produced by the following steps first an upward spread of the impulse through the interatrial septum followed by a downward oriented excitation wave traversing both atrial free walls In the extremity lead the septal component is not manifest The mural excitation proceeding from above down and on the left side earlier than on the right gives rise to the positive P waves We are led to this conclusion because in other instances we have seen similar positive P waves of AVN origin preceded by a small *negative* deflection which we think *represents the upward-directed force originating* in the interatrial septum Whether this force is evinced in the peripheral leads or not depends on its magnitude and direction Figure 10 which is another *example of* experimental AV nodal rhythm with positive P waves in bipolar extremity leads II and III, *demonstrates* early activation of the interatrial septum not evident in peripheral leads

The experiments suggest *the mechanism* of production of upright peripheral P waves in arrhythmias *originating* in the AVN or its vicinity The activation of the atria *proceeds from* above downward in the free walls after the impulse has reached *the* roof of the atria usually by way of the interatrial septum In the extremity leads *this* early septal upward spread may pass unregistered and corresponds to a fraction of time just preceding the onset of the P wave While the AVN takes up the pacemaking function such positive P waves in leads II III and aV_F are encountered experimentally both before and following the ventricular complexes

Positive P waves in leads II and III (or equivalents) have been described in AVN rhythms obtained experimentally and clinically by Scherf and Shookhoff[9] and others (see Scherf s monograph[22]) but no satisfactory explanation of the mechanism of their production has been offered It is suspected that the vertically directed septal components are partially neutralized by their images resulting from the greater conductivity of the blood in the atria Hence they are not recorded peripherally or are recorded poorly (Chapter 12)

which the atria are activated in A-V nodal rhythms The problem was approached by simultaneous multiple registration of the local atrial potentials

The most commonly encountered type of AVN activity successive to the elimination of the SAN is the well known simultaneous activation of the atria and ventricles, with the P wave buried in the QRS complex of the bipolar standard leads *In this type, the first region of the atria to be activated is the interatrial septum*, the free walls follow closely, there being no region of delay (fig 5) The complete activation of the atria *is accomplished in a shorter period of time than is the case when the SAN* is the pacemaker because excitation spreads almost simultaneously from the AVN through the septum and the free atrial walls, thus cutting the normal activation time of the atria in half [31] The left atrium is almost *always activated somewhat earlier than the right* this left atrial precedence being observed in other types of A V nodal arrhythmias as well [3]

In the A V nodal rhythm characterized by an inverted P wave in leads II and III preceding the ventricular complex the first atrial area to be demonstrably activated is usually again the atrial septum, this is followed by the left and, lastly, by the right atrial free wall However, the duration of the P wave is prolonged as the result of delayed activation of the atrial walls Figure 6 illustrates the difference between the activation of the anterior aspect of the right atrium during normal sinus rhythm and during A V nodal rhythm of the type just described after the SAN had been removed It can be seen that during sinus rhythm the activation proceeds from above downward, slightly before and after the onset of the peripheral P wave With the pacemaker in the AVN, the same points on the anterior right atrial wall are activated in a reversed order and late in atrial electrical systole Actually this area is excited during the second half of the peripheral P wave at a time when other atrial areas (interatrial septum *left atrium) have already been depolarized*

The tracing reproduced in figure 7 shows a similar type of A V nodal rhythm (an inverted P wave precedes the ventricular complex) but the *pattern of activation is somewhat different The superior area of the right* atrium is activated very late but even depolarization of the interatrial septum and interatrial band (a muscle uniting the roofs of both atria) appears delayed *The earliest activity registered is encountered in the* left atrium (not reproduced)

When the ventricles contract earlier than the atria a negative P wave usually follows the QRS complex *The order of activation in the atria is* about the same as if the negative P wave preceded the QRS Figure 8 exhibits an early depolarization of the interatrial septum and a tardy appearance of activity in the right atrium *especially in its superior parts*

After radical removal of the SAN and the surrounding tissue, a positive

P wave in leads II and III sometimes appears if during the ensuing AVN rhythm of the commonest type (i e , simultaneous excitation of the atria and ventricles) a small amount of epinephrine is injected into the atrial musculature in the region of the AVN Figure 9 is an example of the phenomenon The form of the P wave in lead II does not substantially differ from that of a normal P wave however the sequence of activation in the atria is at great variance with the normal pattern The tip of the left appendage (in sinus rhythm the last point to be activated) is depolarized far earlier than the right atrium which instead of being the first now is the last in the order of excitation, close to or coinciding with the termination of the reference P wave

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The experiments suggest the mechanism of production of upright peripheral P waves in arrhythmias originating in the AVN or its vicinity The activation of the atria proceeds from above downward in the free walls after the impulse has reached the roof of the atria usually by way of the interatrial septum In the *extremity leads* this early septal upward spread may pass unregistered and corresponds to a fraction of time just preceding the onset of the P wave While the AVN takes up the pacemaking function such positive P waves in leads II III and aV_F are encountered experimentally both before and following the ventricular complexes

Positive P waves in leads II and III (or equivalents) have been described in AVN rhythms obtained experimentally and clinically by Scherf and Shookhoff[8] and others (see Scherf s monograph[17]) but no satisfactory explanation of the mechanism of their production has been offered It is suspected that the vertically directed septal components are partially neutralized by their images resulting from the greater conductivity of the blood in the atria Hence they are not recorded peripherally or are recorded poorly (Chapter 12)

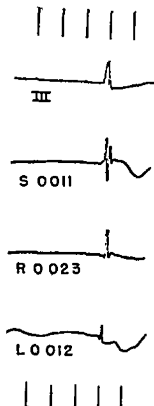


Fig 5

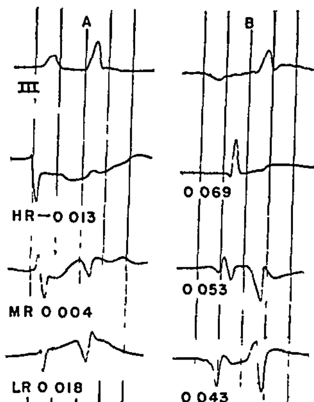


Fig 6

Fig 5 Dog exp 51 A V nodal rhythm with the P wave buried in the QRS complex *Upper tracing lead III (with peak of R as reference point)* Time of spike in lower three tracings (all near bipolar or differential leads) from above downward interatrial septum (S) 0 011 sec upper right atrium (R) 0 023 sec mid left atrium (L) 0 012 sec Paper speed 60 mm *per sec time lines 0 1 sec In this figure and the* following ones tracings obtained by recording from atrial epicardium or septal endocardium simultaneous with a peripheral reference lead are reproduced The electrograms were secured either by means of near bipolar (differential) or unipolar leads The apex of the principal deflection (spike) in the differential lead has been taken as a signal of arrival of the excitatory process at the explored point In unipolar direct leads we consider the end of the most rapid component of the intrinsic deflection as the comparable signal [23, 24] Unless stated otherwise the electrograms were taken after the SAN had been removed surgically and the AVN had become the pacemaker

Fig 6 Dog exp 33 A before B after removal of SAN Normal sinus rhythm in A is replaced by A V nodal rhythm with an inverted P wave preceding the QRS complex in B The sequence of activation in the explored points of the right atrium *is reversed when the impulse originates in the AVN Upper tracing lead III* Activation time in lower three tracings from above downward upper right atrium (HR differential lead) *A* —0 013 sec *B* 0 069 sec mid right atrium (MR unipolar lead) *A* 0 004 sec *B* 0 053 sec low right atrium (LR unipolar lead) *A* 0 018 sec *B* 0 043 sec all measured from the beginning of the P wave in lead III Paper speed 120 mm per sec time lines approximately 0 05 sec The minus sign preceding a number in this figure and subsequent ones means that excitation of the explored point takes place ahead of the reference point

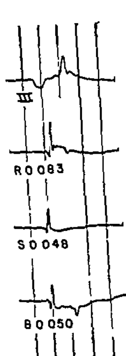


Fig 7

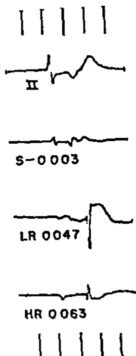


Fig 8

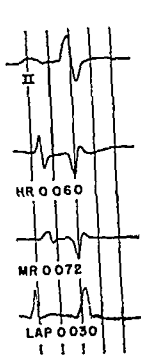


Fig 9

Fig 7 Dog exp 45 A V nodal rhythm. A negative I wave precedes the ventricular complex in lead III Activation time in lower three tracings (all differential lead) from above downward upper right atrium (R) 0 083 sec interatrial septum (S) 0 048 sec interatrial band or interatrial horizontal fa cicle (B) 0 050 sec measured from beginning of the P wave in lead III Paper speed 60 mm per sec time lines 0 1 sec

Fig 8 Dog exp 51 A V nodal rhythm with an inverted P wave following the ventricular complex Upper tracing lead II Time of atrial excitation in lower three differential leads from above downward interatrial septum (S) —0 003 sec inferior right atrium (LR) 0 047 sec upper right atrium (HR) 0 063 sec measured from the beginning of the I wave in lead II Paper speed 60 mm per sec

Fig 9 Dog exp 30 During an A V nodal rhythm with simultaneous atrial and ventricular beat epinephrine solution was injected into the region of the AVN The A V nodal rhythm changed the atria were activated ahead of the ventricles and the P waves were positive in all three bipolar extremity leads However the sequence of activation of the atria appeared to be highly abnormal the left atrium was activated before the right atrium which in the explored anterior surface was depolarized late in atrial systole Upper tracing lead II Activation time in lower three tracings (all unipolar leads) from above downward upper right atrium (HR) 0 060 sec mid right atrium (MR) 0 072 sec left appendage (LAP polarity reversed) 0 030 sec measured from the beginning of the P wave in lead II Paper speed 120 mm per sec time lines 0 05 sec



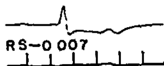








Fig 10 Dog exp 79 A V nodal rhythm with an upright P wave in front of the QRS deflection in all bipolar extremity leads the interatrial septum is depolarized *before* the onset of the P wave in lead II First tracing lead II second to fifth tracings leads obtained from the endocardial surface of the interatrial septum the upper two from the left (LS) the lower two from the right side (RS) of the septum All electrograms registered by differential leads Times of excitation (from above downward) −0 016 −0 018 −0 003 and −0 007 sec measured from the beginning of the P wave in lead II Paper speed 100 mm per sec time lines 0 05 sec



New light has been shed on the complicated function of the AVN by two recent papers of considerable importance Van der Kooi Durrer and associates,[19] using a sensitive recording system have *shown in experiments* on dogs that the AVN develops a peculiar local electrical activity after the arrival of the impulse from the SAN through the atrial musculature This activity is inscribed in the form of multiple fast deflections which closely resemble similar vibrations recorded in the region of the SAN

However whereas the latter precedes the P wave in lead II by about 25 msec the former begins in the second half of that deflection The time difference between the commencement of the two sets of vibrations* is only 36 msec The early activation of the AVN proves that the factor responsible for the long duration of the normal P R interval, if the atria are of normal size is not in the junction between the atrial and the AVN specific musculature

The second contribution of consequence is Grant s[3] who views the relation of the SAN to the AVN as an interplay of two coupled electronic oscillators of easily disturbed stability Both nodes have their own rhythm which under normal circumstances, is identical since the rate of the AVN oscillator pulls in with that of the SAN In order to be conducted to the ventricle the potential must reach a certain threshold and this is most often accomplished by the summation of two potential (1) the non propagated potential generated in the AVN by the incoming impulse from the SAN (analogous to the local nonpropagated potential produced in a neuromuscular junction which is indispensable for the transmission of the impulse from the motor nerve to the muscle fiber) and (2) the usually subthreshold potential of the oscillations arising in the AVN itself Various AVN dysrhythmias and disturbances of rhythm of other types can be explained on the basis of Grant s theory as being due to an enhanced AVN rhythmicity an elevated threshold in the AVN increased voltage of the AVN oscillations or a combination of these elements Undoubtedly there is more harmony with present-day knowledge of impulse transmission in Grant s interpretation than in current explanations The validity of the theory could be tested experimentally by van der Kooi s and Durrer s[48] technique of obtaining local potentials in the AVN

In the space allotted it has not been possible to discuss all dysrhythmias ascribed to the atrioventricular node to elaborate on its possible role in circus rhythm or to review the innumerable publications dealing with the functions of this important structure Only the most salient features of the subject have been mentioned and the most pertinent contributions quoted It has been our aim to present the A V nodal dysrhythmias in the light of recent investigations which point more and more to the pivotal and not yet sufficiently explored role of the AVN in the rhythmic coordination of the heart beat

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PART V

17 Summary and Conclusions

CHARLES E KOSSMANN, M D

THE ADVANCES in electrocardiography made during the period 1946–56 that are thought to be of the greatest present and future significance have been presented here under four categories the source of potential, the conducting medium, the spread of excitation and of recovery, and rhythms

I Source of Potential

The form and magnitude of the transmembrane action potential as recorded by the intracellular microelectrode have been reviewed and summarized An understanding of the basis for the potential, in terms of the Nernst equation, both in the resting and active state requires a consideration not only of ionic concentration gradients but of ionic flux densities across the membrane The principal factor involved appears to be the excess of ionic flux of Na into the cell which neutralizes and reverses the electrical significance of the concentration gradient of this ion in the resting state This explanation presupposes the existence of an active mechanism for extrusion of the Na ion in non ionic form (Chapter 2) The gradient of K ions in the resting state is probably secondary to the active carriage of Na

Modification of the form and magnitude of the transmembrane potential by means of a variety of agents has demonstrated in certain instances an uncoupling of the action potential and the contractile function of the myocardium With digitalis the former can be modified without effect on the latter, stretching of the muscle causes the opposite type of response Triiodothyronine will produce alternation of various components of the transmembrane action potential demonstrating that electrical alternans occurs at the membrane level

II The Conducting Medium

The heart is surrounded externally by a medium which has approximately the same specific resistance as the myocardium itself but internally by a medium (blood) which has a specific resistance approximately one tenth as great In the case of the isolated excitable cell it can be demonstrated that a lead from a surrounding conductive medium may yield a record

which is in form, the first or second derivative of the monophasic action potential depending upon the extent of the medium and the method of leading. The principles apply to the heart as a whole and help to explain the origin of the multiphasic clinical record (Chapter 1)

The irregular boundary of the external medium of the heart, the eccentric location of the latter in this medium and the greater conductivity of the internal medium give rise to a variety of problems relating to the concepts of the image space and electric images

Image space is an imaginary boundary defined by the loci of the image vectors (lead vectors, correction coefficients, transfer function, transfer impedances). The image (lead) vector is a factor by means of which the expected distortion of any lead from a finite heterogeneous medium containing an eccentric source of current may be corrected. When lead vectors are substituted for the sides of Einthoven's triangle, a generalization results which is known as Burger's triangle. In the latter, lead III is usually longer than the other two leads as determined on models

The lead vector concept requires the retention of the hypothesis that the heart behaves as a dipolar source of current (Chapter 7). There is much evidence against this. To overcome this restriction the lead vector for each point in the heart is determined from the intensity of the current at *that* point produced by reciprocal stimulation of the particular lead with a unit source of current. The method yields a generalization of the lead vector concept and is called the lead field concept (McFee and Johnston)

In any attempt to quantitate leads the *movement of the heart center* during excitation and recovery remains an unsolved restricting influence

A variety of orthogonalized and normalized lead systems or *reference frames* have been designed to yield the corrected spatial vectorcardiogram (Chapter 6). Those reviewed include the B_1, R_2 and W_4'' *systems of Burger* and his associates, the lead field system of McFee and Johnston, the *SVEC III* system of Schmitt and his associates, the precordial *system and R L F B* systems of Frank (the latter comparable to the W_4'' system and both being the corrected tetrahedral frame of *Wilson, Johnston* and Rossmann), and the Helm modification of Frank's *precordial system*

There is a fair degree of similarity *in form* of the spatial vectorcardiograms obtained by the various *corrected frames of reference*. It remains to be proven that these have any *superiority over* more conventional methods of leading from the viewpoint of clinical diagnosis

A device whereby correction factors for any given set of leads can be varied at will is called a universal vectorcardiograph. Another by means of which the various loops or *parts may* be separately recorded is called a differential vectorcardiograph

A review of all the *empirical leads* which have been used is presented with the conclusion that such special leads are *only rarely* of unique diag

nostic value in clinical electrocardiography (Chapter 8) An exception are the esophageal leads which may yield useful information when the nature of activity in the atria is not obvious from surface leads

III Spread of Excitation and of Recovery Normal and Abnormal

A review of available data on endocardial, myocardial, and epicardial leads in man indicates that some differences exist in the spread of excitation in comparison to the findings Lewis described in dogs (Chapter 9) Most significant is the excitation of a portion of the basal septum from below upward The data on intramural leads is so variable that physiologic and clinical interpretations stemming from the absence or diminutive size of the R wave in subendocardial leads must be made with caution Interpretation of injury phenomena observed on the surface and interior of animal hearts exposed to air have not included adequate consideration of the effect of electric images on the records obtained

In a comprehensive review of the problems relating to normal and abnormal excitation of the ventricles in man, consideration of the problem from the standpoint of conduction rather than of block reveals variations in normal subjects which are indistinguishable from those regarded as abnormal (Chapter 10) By means of high gain, fast speed records it is demonstrated that there are variations in normal subjects depending upon the side of the interventricular septum excited earliest and the side of the remaining ventricular mass excited last Of the four possible categories the one in which there is initial left septal and late right mural excitation is by far the most frequent (85 per cent) in normal man

The electrocardiographic effects of experimental myocardial injury have often been interpreted without adequate consideration of the effects of electric images resulting from existing or experimentally produced contiguity of conducting media with different specific resistances (Chapter 12) The conductivities of the adjacent media, the shape of the boundary between them the location and orientation of the source of current are all important in determining the magnitude of the recorded potential

In congenital heart disease the cardiac malformation itself affects the electrocardiogram only exceptionally It is the effects of the anomaly—hypertrophy dilatation atrophy, block ischemia—which usually produce the electrocardiographic abnormalities Since certain malformations have a tendency to provoke a certain type of response in the heart a corresponding alteration in the electrocardiogram can be expected and is often found Exceptions are so numerous however that a precise diagnosis of a congenital cardiopathy can only be made by evaluating the electrocardiogram in the light of results of other diagnostic procedures

The less than generally believed correlation between the electrocardiogram and hypertrophy of one or the other ventricular chambers has been

restated The suggestive relation between certain hemodynamic states and the configuration of the electrocardiogram is an approach to the problem which shows considerable promise but which requires further study before being given general clinical acceptance

If the gradient or flux of ions across the membrane at the end of the relative refractory period is not the same as in the resting state an after potential will result It is probable that the eventual dissipation of this after potential is responsible for the U wave in clinical records although other origins have been suggested (Chapter 11) From the clinical point of view, it is noteworthy that different concentrations of serum potassium affect the T wave and the U wave in opposite directions and that drugs which ordinarily increase cardiac excitability (epinephrine, calcium digitalis) also augment the U wave

IV Rhythms

The effects of heart rate temperature vagal stimulation, chemical mediators ions and drugs on the various parameters of cardiac excitability have been reviewed A number of antiarrhythmic agents have been evaluated in terms of their effect on the same excitability parameters and on the diastolic threshold The data disclose that no single variable is uniformly related to the production of vulnerability to multiple firing or fibrillation Although the antiarrhythmic agents affect excitability by raising the diastolic threshold and prolonging the refractory period these effects are not invariably proportional to the antiarrhythmic action of the specific drug or dosage Other actions appear to play an important role in the production and prevention of enhanced myocardial excitability

Individual types of atrioventricular nodal arrhythmias were produced in dogs by surgical removal of the sinoatrial node (Chapter 16) Postoperatively various sequences of atrial depolarization could be identified Usually the left atrium was activated earlier than the right When the P wave and the QRS deflections were simultaneous the interatrial septum and the free walls of both atria were activated simultaneously

Injection of epinephrine into the region of the atrioventricular node was used to provoke an A V nodal rhythm characterized by upright P waves in bipolar extremity leads preceding QRS by a short or normal P R interval In such instances endocardial leads revealed that the impulse spread initially upward in the interatrial septum and subsequently downward in the free walls of the atria The septal component was often not manifest in the extremity leads possibly due to the existence of electric images of reverse sign in the highly conducting blood filled atrial cavities (Chapter 12) The observation strengthens the belief that upright P waves may occur in leads II and III of clinical records even when the pacemaker is in the atrioventricular node

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